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(54) Title: HUMAN TRANSCRIPTIONAL REGULATOR MOLECULES			
(57) Abstract			
The invention provides human transcriptional regulator molecules (HTRM) and polynucleotides which identify and encode HTRM. The invention also provides expression vectors, host cells, antibodies, agonists and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders associated with expression of HTRM.			

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HUMAN TRANSCRIPTIONAL REGULATOR MOLECULES

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TECHNICAL FIELD

This invention relates to nucleic acid and amino acid sequences of human transcriptional regulator molecules and to the use of these sequences in the diagnosis, treatment, and prevention of cell proliferative and immune disorders.

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BACKGROUND OF THE INVENTION

Differential control of gene expression is essential to the growth and development of all multicellular organisms. Although gene expression can be controlled at many steps along the path from DNA to protein, the major control point for most genes is at the initiation of transcription. This critical step is regulated both positively and negatively by a combination of general and tissue specific transcription factors, the majority of which function to regulate transcription of one or more target genes.

Mutations in transcription factors (TFs) contribute to oncogenesis. This is probably due to the role of transcription factors on the expression of genes involved in cell proliferation. For example, mutations in transcription factors encoded by proto-oncogenes, such as Fos, Jun, Myc, Rel, and Spi-1, may be oncogenic due to increased stimulation of cell proliferation. Conversely, mutations in transcription factors encoded by tumor suppressor genes, such as p53, RB1, and WT1, may be oncogenic due to decreased inhibition of cell proliferation. (Latchman, D. (1995) Gene Regulation: A Eukaryotic Perspective, Chapman and Hall, London, UK, pp 242-255.)

Many transcription factors are modular proteins that contain separate domains for DNA binding and transcriptional regulation. The DNA binding domain interacts with specific DNA sequences (control elements) near to or within the promoter region of the gene. This interaction brings the regulatory domain of the TF into a position where it can interact with other proteins to stimulate or repress transcription. Many TFs require dimerization or multimerization to be fully functional. Five different types of transcription factors have been described based on five well characterized structural motifs. These five types are the helix-turn-helix, zinc finger, leucine zipper, and helix-loop-helix (HLH) proteins and the steroid-hormone receptors.

The helix-turn-helix motif consists of two α helices held at a fixed angle. The two helices are connected by a short chain of amino acids, which represents the "turn". The more carboxyl-terminal helix is called the recognition helix and fits into the major groove of the DNA double helix. The recognition helix, whose amino acid side chains differ from protein to protein, plays an

important role in recognizing the specific DNA sequence to which the protein binds. All of the helix-turn-helix proteins bind DNA as dimers in which the two copies of the recognition helix are separated by exactly one turn of the DNA helix. Homeodomain proteins are a special class of helix-turn-helix protein. The homeodomain is folded into three α helices which are packed tightly together by hydrophobic interactions. Helices two and three closely resemble the helix-turn-helix motif, with the third helix acting as the recognition helix. Proteins containing homeodomain motifs often function as developmental switches.

The zinc finger motif consists of an α helix and antiparallel β sheet held together by a zinc atom. The zinc finger motif is usually repeated in a tandem array within a protein, such that the α helix of each zinc finger in the protein makes contact with the major groove of the DNA double helix. This repeated contact between the protein and the DNA produces a strong and specific DNA-protein interaction. The strength and specificity of the interaction can be regulated by the number of zinc finger motifs within the protein.

The leucine zipper motif consists of a single α helix which is involved in both protein dimerization and DNA binding. Two proteins containing leucine zippers can dimerize by interactions between hydrophobic amino acid residues, commonly leucines, that extend from one side of their respective α helices. In this way, the α helices of each protein monomer dimerize to form a short coiled-coil. Just beyond this coiled-coil, the two α helices separate to form a Y-shaped structure which contacts the major groove of the DNA. Leucine zipper proteins may form homodimers, in which the two protein monomers are identical, or heterodimers, in which the two protein monomers are different. The specificity of DNA binding depends on the dimer formed, since each protein monomer has distinct DNA-binding specificities.

The helix-loop-helix (HLH) motif consists of a short α helix connected by a loop to a second, longer α helix. The flexible loop allows the two helices to fold back and pack together. As with the leucine zipper, the HLH motif is involved in both protein dimerization and DNA binding. The dimers can be homodimers or heterodimers, thus increasing the repertoire of DNA-binding sites to which HLH proteins can bind.

The steroid-hormone receptors contain a motif composed of two perpendicular α helices. In the absence of ligand the steroid-hormone receptors assume a conformation which sequesters the α helices. Binding of ligand, commonly steroid hormones, thyroid hormones, retinoids, or vitamin D, to the receptor causes a conformational change which exposes the α helices. The first α helix contains about seventy residues and includes eight conserved cysteines. This helix fits into the major groove of the DNA double helix and enables DNA-receptor binding. The second α helix provides for protein dimerization. As with leucine zipper and HLH proteins, both homodimers and heterodimers may be formed by steroid-hormone receptors.

Hundreds of regulatory proteins from a wide variety of organisms have been identified. Most of these proteins have at least one of the common structural motifs described. However, several important regulatory proteins, including the p53 tumor suppressor, have a unique structure not shared with other known regulatory molecules. (Faisst, S. and S. Meyer (1992) Nucl. Acids Res. 20:3-26.) Moreover, other domains of the regulatory proteins often form crucial contacts with the DNA, thereby affecting binding specificity. Accessory proteins can also provide important interactions which may convert a particular regulatory protein from an activator to a repressor, from a repressor to an activator, or it may prevent DNA binding by the regulatory protein completely.

The discovery of new human transcriptional regulator molecules and the polynucleotides encoding them satisfies a need in the art by providing new compositions which are useful in the diagnosis, prevention, and treatment of cell proliferative and immune disorders.

SUMMARY OF THE INVENTION

The invention features substantially purified polypeptides, human transcriptional regulator molecules, referred to collectively as "HTRM". In one aspect, the invention provides a substantially purified polypeptide comprising an amino acid sequence selected from the group consisting of

SEQ ID NO:1-65, and fragments thereof.

The invention further provides a substantially purified variant having at least 90% amino acid identity to at least one of the amino acid sequences selected from the group consisting of SEQ ID

NO:1-65, and fragments thereof. The invention also provides an isolated and purified polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof. The invention also includes an isolated and purified polynucleotide variant having at least 70% polynucleotide sequence identity to the polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting

of SEQ ID NO:1-65, and fragments thereof.

Additionally, the invention provides an isolated and purified polynucleotide which hybridizes under stringent conditions to the polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof. The invention also provides an isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide encoding the polypeptide comprising the amino

acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof.

The invention also provides an isolated and purified polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:66-130, and fragments thereof. The invention further provides an isolated and purified polynucleotide variant having at least 70% polynucleotide sequence identity to the polynucleotide sequence selected from the group consisting of SEQ ID NO:66-130, and fragments thereof. The invention also provides an isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:66-130, and fragments thereof.

The invention also provides a method for detecting a polynucleotide in a sample containing nucleic acids, the method comprising the steps of (a) hybridizing the complement of the polynucleotide sequence to at least one of the polynucleotides of the sample, thereby forming a hybridization complex; and (b) detecting the hybridization complex, wherein the presence of the hybridization complex correlates with the presence of a polynucleotide in the sample. In one aspect, the method further comprises amplifying the polynucleotide prior to hybridization.

The invention further provides an expression vector containing at least a fragment of the polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof. In another aspect, the expression vector is contained within a host cell.

The invention also provides a method for producing a polypeptide, the method comprising the steps of: (a) culturing the host cell containing an expression vector containing at least a fragment of a polynucleotide under conditions suitable for the expression of the polypeptide; and (b) recovering the polypeptide from the host cell culture.

The invention also provides a pharmaceutical composition comprising a substantially purified polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof, in conjunction with a suitable pharmaceutical carrier.

The invention further includes a purified antibody which binds to a polypeptide selected from the group consisting of SEQ ID NO:1-65, and fragments thereof. The invention also provides a purified agonist and a purified antagonist to the polypeptide.

The invention also provides a method for treating or preventing a disorder of cell proliferation associated with decreased expression or activity of HTRM, the method comprising administering to a subject in need of such treatment an effective amount of a pharmaceutical composition comprising a substantially purified polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof, in conjunction with a suitable pharmaceutical carrier.

The invention also provides a method for treating or preventing a disorder of cell proliferation associated with increased expression or activity of HTRM, the method comprising administering to a subject in need of such treatment an effective amount of an antagonist of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof.

BRIEF DESCRIPTION OF THE TABLES

Table 1 shows nucleotide and polypeptide sequence identification numbers (SEQ ID NO), clone identification numbers (clone ID), cDNA libraries, and cDNA fragments used to assemble full-length sequences encoding HTRM.

Table 2 shows features of each polypeptide sequence including potential motifs, homologous sequences, and methods and algorithms used for identification of HTRM.

Table 3 shows the tissue-specific expression patterns of each nucleic acid sequence as determined by northern analysis, diseases, disorders, or conditions associated with these tissues, and the vector into which each cDNA was cloned.

Table 4 describes the tissues used to construct the cDNA libraries from which Incyte cDNA clones encoding HTRM were isolated.

Table 5 shows the programs, their descriptions, references, and threshold parameters used to analyze HTRM.

DESCRIPTION OF THE INVENTION

Before the present proteins, nucleotide sequences, and methods are described, it is understood that this invention is not limited to the particular machines, materials and methods described, as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise. Thus, for example, a reference to "a host cell" includes a plurality of such host cells, and a reference to "an antibody" is a reference to one or more antibodies and equivalents thereof known to those skilled in the art, and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any machines, materials, and methods similar or equivalent to those described herein can be used to practice or test the present invention, the preferred machines, materials and

methods are now described. All publications mentioned herein are cited for the purpose of describing and disclosing the cell lines, protocols, reagents and vectors which are reported in the publications and which might be used in connection with the invention. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of

5 prior invention.

DEFINITIONS

"HTRM" refers to the amino acid sequences of substantially purified HTRM obtained from any species, particularly a mammalian species, including bovine, ovine, porcine, murine, equine, and preferably the human species, from any source, whether natural, synthetic,

10 semi-synthetic, or recombinant.

The term "agonist" refers to a molecule which, when bound to HTRM, increases or prolongs the duration of the effect of HTRM. Agonists may include proteins, nucleic acids, carbohydrates, or any other molecules which bind to and modulate the effect of HTRM.

An "allelic variant" is an alternative form of the gene encoding HTRM. Allelic variants

15 may result from at least one mutation in the nucleic acid sequence and may result in altered mRNAs or in polypeptides whose structure or function may or may not be altered. Any given natural or recombinant gene may have none, one, or many allelic forms. Common mutational changes which give rise to allelic variants are generally ascribed to natural deletions, additions, or substitutions of nucleotides. Each of these types of changes may occur alone, or in combination

20 with the others, one or more times in a given sequence.

"Altered" nucleic acid sequences encoding HTRM include those sequences with deletions, insertions, or substitutions of different nucleotides, resulting in a polynucleotide the same as HTRM or a polypeptide with at least one functional characteristic of HTRM. Included within this definition are polymorphisms which may or may not be readily detectable using a particular

25 oligonucleotide probe of the polynucleotide encoding HTRM, and improper or unexpected hybridization to allelic variants, with a locus other than the normal chromosomal locus for the polynucleotide sequence encoding HTRM. The encoded protein may also be "altered," and may contain deletions, insertions, or substitutions of amino acid residues which produce a silent change and result in a functionally equivalent HTRM. Deliberate amino acid substitutions may be made

30 on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the biological or immunological activity of HTRM is retained. For example, negatively charged amino acids may include aspartic acid and glutamic acid, positively charged amino acids may include lysine and arginine, and amino acids with uncharged polar head groups having similar hydrophilicity values may include leucine, isoleucine,

35 and valine; glycine and alanine; asparagine and glutamine; serine and threonine; and

phenylalanine and tyrosine.

The terms "amino acid" or "amino acid sequence" refer to an oligopeptide, peptide, polypeptide, or protein sequence, or a fragment of any of these, and to naturally occurring or synthetic molecules. In this context, "fragments," "immunogenic fragments," or "antigenic fragments" refer to fragments of HTRM which are preferably at least 5 to about 15 amino acids in length, most preferably at least 14 amino acids, and which retain some biological activity or immunological activity of HTRM. Where "amino acid sequence" is recited to refer to an amino acid sequence of a naturally occurring protein molecule, "amino acid sequence" and like terms are not meant to limit the amino acid sequence to the complete native amino acid sequence associated with the recited protein molecule.

"Amplification" relates to the production of additional copies of a nucleic acid sequence. Amplification is generally carried out using polymerase chain reaction (PCR) technologies well known in the art.

The term "antagonist" refers to a molecule which, when bound to HTRM, decreases the amount or the duration of the effect of the biological or immunological activity of HTRM. Antagonists may include proteins, nucleic acids, carbohydrates, antibodies, or any other molecules which decrease the effect of HTRM.

The term "antibody" refers to intact molecules as well as to fragments thereof, such as Fab, F(ab')₂, and Fv fragments, which are capable of binding the epitopic determinant. Antibodies that bind HTRM polypeptides can be prepared using intact polypeptides or using fragments containing small peptides of interest as the immunizing antigen. The polypeptide or oligopeptide used to immunize an animal (e.g., a mouse, a rat, or a rabbit) can be derived from the translation of RNA, or synthesized chemically, and can be conjugated to a carrier protein if desired. Commonly used carriers that are chemically coupled to peptides include bovine serum albumin, thyroglobulin, and keyhole limpet hemocyanin (KLH). The coupled peptide is then used to immunize the animal.

The term "antigenic determinant" refers to that fragment of a molecule (i.e., an epitope) that makes contact with a particular antibody. When a protein or a fragment of a protein is used to immunize a host animal, numerous regions of the protein may induce the production of antibodies which bind specifically to antigenic determinants (given regions or three-dimensional structures on the protein). An antigenic determinant may compete with the intact antigen (i.e., the immunogen used to elicit the immune response) for binding to an antibody.

The term "antisense" refers to any composition containing a nucleic acid sequence which is complementary to the "sense" strand of a specific nucleic acid sequence. Antisense molecules may be produced by any method including synthesis or transcription. Once introduced into a cell, the complementary nucleotides combine with natural sequences produced by the cell to form

duplexes and to block either transcription or translation. The designation "negative" can refer to the antisense strand, and the designation "positive" can refer to the sense strand.

The term "biologically active," refers to a protein having structural, regulatory, or biochemical functions of a naturally occurring molecule. Likewise, "immunologically active" refers to the capability of the natural, recombinant, or synthetic HTRM, or of any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

The terms "complementary" or "complementarity" refer to the natural binding of polynucleotides by base pairing. For example, the sequence "5' A-G-T 3'" bonds to the complementary sequence "3' T-C-A 5'." Complementarity between two single-stranded molecules may be "partial," such that only some of the nucleic acids bind, or it may be "complete," such that total complementarity exists between the single stranded molecules. The degree of complementarity between nucleic acid strands has significant effects on the efficiency and strength of the hybridization between the nucleic acid strands. This is of particular importance in amplification reactions, which depend upon binding between nucleic acids strands, and in the design and use of peptide nucleic acid (PNA) molecules.

A "composition comprising a given polynucleotide sequence" or a "composition comprising a given amino acid sequence" refer broadly to any composition containing the given polynucleotide or amino acid sequence. The composition may comprise a dry formulation or an aqueous solution. Compositions comprising polynucleotide sequences encoding HTRM or fragments of HTRM may be employed as hybridization probes. The probes may be stored in freeze-dried form and may be associated with a stabilizing agent such as a carbohydrate. In hybridizations, the probe may be deployed in an aqueous solution containing salts (e.g., NaCl), detergents (e.g., sodium dodecyl sulfate; SDS), and other components (e.g., Denhardt's solution, dry milk, salmon sperm DNA, etc.).

"Consensus sequence" refers to a nucleic acid sequence which has been resequenced to resolve uncalled bases, extended using XL-PCR kit (Perkin-Elmer, Norwalk CT) in the 5' and/or the 3' direction, and resequenced, or which has been assembled from the overlapping sequences of more than one Incyte Clone using a computer program for fragment assembly, such as the GELVIEW Fragment Assembly system (GCG, Madison WI). Some sequences have been both extended and assembled to produce the consensus sequence.

The term "correlates with expression of a polynucleotide" indicates that the detection of the presence of nucleic acids, the same or related to a nucleic acid sequence encoding HTRM, by northern analysis is indicative of the presence of nucleic acids encoding HTRM in a sample, and thereby correlates with expression of the transcript from the polynucleotide encoding HTRM.

A "deletion" refers to a change in the amino acid or nucleotide sequence that results in the absence of one or more amino acid residues or nucleotides.

The term "derivative" refers to the chemical modification of a polypeptide sequence, or a polynucleotide sequence. Chemical modifications of a polynucleotide sequence can include, for example, replacement of hydrogen by an alkyl, acyl, or amino group. A derivative polynucleotide encodes a polypeptide which retains at least one biological or immunological function of the natural molecule. A derivative polypeptide is one modified by glycosylation, pegylation, or any similar process that retains at least one biological or immunological function of the polypeptide from which it was derived.

10 The term "similarity" refers to a degree of complementarity. There may be partial similarity or complete similarity. The word "identity" may substitute for the word "similarity." A partially complementary sequence that at least partially inhibits an identical sequence from hybridizing to a target nucleic acid is referred to as "substantially similar." The inhibition of hybridization of the completely complementary sequence to the target sequence may be examined
15 using a hybridization assay (Southern or northern blot, solution hybridization, and the like) under conditions of reduced stringency. A substantially similar sequence or hybridization probe will compete for and inhibit the binding of a completely similar (identical) sequence to the target sequence under conditions of reduced stringency. This is not to say that conditions of reduced stringency are such that non-specific binding is permitted, as reduced stringency conditions
20 require that the binding of two sequences to one another be a specific (i.e., a selective) interaction. The absence of non-specific binding may be tested by the use of a second target sequence which lacks even a partial degree of complementarity (e.g., less than about 30% similarity or identity). In the absence of non-specific binding, the substantially similar sequence or probe will not hybridize to the second non-complementary target sequence.

25 The phrases "percent identity" or "% identity" refer to the percentage of sequence similarity found in a comparison of two or more amino acid or nucleic acid sequences. Percent identity can be determined electronically, e.g., by using the MEGALIGN program (DNASTAR, Madison WI) which creates alignments between two or more sequences according to methods selected by the user, e.g., the clustal method. (See, e.g., Higgins, D.G. and P.M. Sharp (1988)
30 Gene 73:237-244.) The clustal algorithm groups sequences into clusters by examining the distances between all pairs. The clusters are aligned pairwise and then in groups. The percentage similarity between two amino acid sequences, e.g., sequence A and sequence B, is calculated by dividing the length of sequence A, minus the number of gap residues in sequence A, minus the number of gap residues in sequence B, into the sum of the residue matches between sequence A
35 and sequence B, times one hundred. Gaps of low or of no similarity between the two amino acid

sequences are not included in determining percentage similarity. Percent identity between nucleic acid sequences can also be counted or calculated by other methods known in the art, e.g., the Jotun Hein method. (See, e.g., Hein, J. (1990) *Methods Enzymol.* 183:626-645.) Identity between sequences can also be determined by other methods known in the art, e.g., by varying

5 hybridization conditions.

“Human artificial chromosomes” (HACs) are linear microchromosomes which may contain DNA sequences of about 6 kb to 10 Mb in size, and which contain all of the elements required for stable mitotic chromosome segregation and maintenance.

The term “humanized antibody” refers to antibody molecules in which the amino acid
10 sequence in the non-antigen binding regions has been altered so that the antibody more closely resembles a human antibody, and still retains its original binding ability.

“Hybridization” refers to any process by which a strand of nucleic acid binds with a complementary strand through base pairing.

The term “hybridization complex” refers to a complex formed between two nucleic acid
15 sequences by virtue of the formation of hydrogen bonds between complementary bases. A hybridization complex may be formed in solution (e.g., C_0t or R_0t analysis) or formed between one nucleic acid sequence present in solution and another nucleic acid sequence immobilized on a solid support (e.g., paper, membranes, filters, chips, pins or glass slides, or any other appropriate substrate to which cells or their nucleic acids have been fixed).

20 The words “insertion” or “addition” refer to changes in an amino acid or nucleotide sequence resulting in the addition of one or more amino acid residues or nucleotides, respectively, to the sequence found in the naturally occurring molecule.

“Immune response” can refer to conditions associated with inflammation, trauma, immune disorders, or infectious or genetic disease, etc. These conditions can be characterized by
25 expression of various factors, e.g., cytokines, chemokines, and other signaling molecules, which may affect cellular and systemic defense systems.

The term “microarray” refers to an arrangement of distinct polynucleotides on a substrate.

The terms “element” or “array element” in a microarray context, refer to hybridizable polynucleotides arranged on the surface of a substrate.

30 The term “modulate” refers to a change in the activity of HTRM. For example, modulation may cause an increase or a decrease in protein activity, binding characteristics, or any other biological, functional, or immunological properties of HTRM.

The phrases “nucleic acid” or “nucleic acid sequence” refer to a nucleotide, oligonucleotide, polynucleotide, or any fragment thereof. These phrases also refer to DNA or
35 RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may

represent the sense or the antisense strand, to peptide nucleic acid (PNA), or to any DNA-like or RNA-like material. In this context, "fragments" refers to those nucleic acid sequences which, when translated, would produce polypeptides retaining some functional characteristic, e.g., antigenicity, or structural domain characteristic, e.g., ATP-binding site, of the full-length
5 polypeptide.

The terms "operably associated" or "operably linked" refer to functionally related nucleic acid sequences. A promoter is operably associated or operably linked with a coding sequence if the promoter controls the translation of the encoded polypeptide. While operably associated or operably linked nucleic acid sequences can be contiguous and in the same reading frame, certain
10 genetic elements, e.g., repressor genes, are not contiguously linked to the sequence encoding the polypeptide but still bind to operator sequences that control expression of the polypeptide.

The term "oligonucleotide" refers to a nucleic acid sequence of at least about 6 nucleotides to 60 nucleotides, preferably about 15 to 30 nucleotides, and most preferably about 20 to 25 nucleotides, which can be used in PCR amplification or in a hybridization assay or
15 microarray. "Oligonucleotide" is substantially equivalent to the terms "amplimer," "primer," "oligomer," and "probe," as these terms are commonly defined in the art.

"Peptide nucleic acid" (PNA) refers to an antisense molecule or anti-gene agent which comprises an oligonucleotide of at least about 5 nucleotides in length linked to a peptide backbone of amino acid residues ending in lysine. The terminal lysine confers solubility to the composition.
20 PNAs preferentially bind complementary single stranded DNA or RNA and stop transcript elongation, and may be pegylated to extend their lifespan in the cell.

The term "sample" is used in its broadest sense. A sample suspected of containing nucleic acids encoding HTRM, or fragments thereof, or HTRM itself, may comprise a bodily fluid; an extract from a cell, chromosome, organelle, or membrane isolated from a cell; a cell; genomic
25 DNA, RNA, or cDNA, in solution or bound to a substrate; a tissue; a tissue print; etc.

The terms "specific binding" or "specifically binding" refer to that interaction between a protein or peptide and an agonist, an antibody, or an antagonist. The interaction is dependent upon the presence of a particular structure of the protein, e.g., the antigenic determinant or epitope, recognized by the binding molecule. For example, if an antibody is specific for epitope "A," the
30 presence of a polypeptide containing the epitope A, or the presence of free unlabeled A, in a reaction containing free labeled A and the antibody will reduce the amount of labeled A that binds to the antibody.

The term "stringent conditions" refers to conditions which permit hybridization between polynucleotides and the claimed polynucleotides. Stringent conditions can be defined by salt
35 concentration, the concentration of organic solvent, e.g., formamide, temperature, and other

conditions well known in the art. In particular, stringency can be increased by reducing the concentration of salt, increasing the concentration of formamide, or raising the hybridization temperature.

The term "substantially purified" refers to nucleic acid or amino acid sequences that are removed from their natural environment and are isolated or separated, and are at least about 60% free, preferably about 75% free, and most preferably about 90% free from other components with which they are naturally associated.

A "substitution" refers to the replacement of one or more amino acids or nucleotides by different amino acids or nucleotides, respectively.

"Substrate" refers to any suitable rigid or semi-rigid support including membranes, filters, chips, slides, wafers, fibers, magnetic or nonmagnetic beads, gels, tubing, plates, polymers, microparticles and capillaries. The substrate can have a variety of surface forms, such as wells, trenches, pins, channels and pores, to which polynucleotides or polypeptides are bound.

"Transformation" describes a process by which exogenous DNA enters and changes a recipient cell. Transformation may occur under natural or artificial conditions according to various methods well known in the art, and may rely on any known method for the insertion of foreign nucleic acid sequences into a prokaryotic or eukaryotic host cell. The method for transformation is selected based on the type of host cell being transformed and may include, but is not limited to, viral infection, electroporation, heat shock, lipofection, and particle bombardment. The term "transformed" cells includes stably transformed cells in which the inserted DNA is capable of replication either as an autonomously replicating plasmid or as part of the host chromosome, as well as transiently transformed cells which express the inserted DNA or RNA for limited periods of time.

A "variant" of HTRM polypeptides refers to an amino acid sequence that is altered by one or more amino acid residues. The variant may have "conservative" changes, wherein a substituted amino acid has similar structural or chemical properties (e.g., replacement of leucine with isoleucine). More rarely, a variant may have "nonconservative" changes (e.g., replacement of glycine with tryptophan). Analogous minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which amino acid residues may be substituted, inserted, or deleted without abolishing biological or immunological activity may be found using computer programs well known in the art, for example, LASERGENE software (DNASTAR).

The term "variant," when used in the context of a polynucleotide sequence, may encompass a polynucleotide sequence related to HTRM. This definition may also include, for example, "allelic" (as defined above), "splice," "species," or "polymorphic" variants. A splice variant may have significant identity to a reference molecule, but will generally have a greater or

lesser number of polynucleotides due to alternate splicing of exons during mRNA processing. The corresponding polypeptide may possess additional functional domains or an absence of domains.

Species variants are polynucleotide sequences that vary from one species to another. The resulting polypeptides generally will have significant amino acid identity relative to each other. A

- 5 polymorphic variant is a variation in the polynucleotide sequence of a particular gene between individuals of a given species. Polymorphic variants also may encompass "single nucleotide polymorphisms" (SNPs) in which the polynucleotide sequence varies by one base. The presence of SNPs may be indicative of, for example, a certain population, a disease state, or a propensity for a disease state.

10 THE INVENTION

The invention is based on the discovery of new human transcriptional regulator molecules (HTRM), the polynucleotides encoding HTRM, and the use of these compositions for the diagnosis, treatment, or prevention of cell proliferative and immune disorders.

- Table 1 lists the Incyte Clones used to derive full length nucleotide sequences encoding HTRM. Columns 1 and 2 show the sequence identification numbers (SEQ ID NO) of the amino acid and nucleic acid sequences, respectively. Column 3 shows the Clone ID of the Incyte Clone in which nucleic acids encoding each HTRM were identified, and column 4, the cDNA libraries from which these clones were isolated. Column 5 shows Incyte clones, their corresponding cDNA libraries, and shotgun sequences. The clones and shotgun sequences are part of the consensus
- 15 nucleotide sequence of each HTRM and are useful as fragments in hybridization technologies.

- The columns of Table 2 show various properties of the polypeptides of the invention: column 1 references the SEQ ID NO; column 2 shows the number of amino acid residues in each polypeptide; column 3, potential phosphorylation sites; column 4, potential glycosylation sites; column 5, the amino acid residues comprising signature sequences and motifs; column 6, the
- 25 identity of each protein; and column 7, analytical methods used to identify each protein through sequence homology and protein motifs.

- The columns of Table 3 show the tissue-specificity and diseases, disorders, or conditions associated with nucleotide sequences encoding HTRM. The first column of Table 3 lists the nucleotide sequence identifiers. The second column lists tissue categories which express HTRM as
- 30 a fraction of total tissue categories expressing HTRM. The third column lists the diseases, disorders, or conditions associated with those tissues expressing HTRM. The fourth column lists the vectors used to subclone the cDNA library.

- The following fragments of the nucleotide sequences encoding HTRM are useful in hybridization or amplification technologies to identify SEQ ID NO:110-130 and to distinguish
- 35 between SEQ ID NO:110-130 and related polynucleotide sequences. The useful fragments are the

fragment of SEQ ID NO:110 from about nucleotide 273 to about nucleotide 317; the fragment of SEQ ID NO:111 from about nucleotide 217 to about nucleotide 261 the fragment of SEQ ID NO:112 from about nucleotide 273 to about nucleotide 308; the fragment of SEQ ID NO:113 from about nucleotide 163 to about nucleotide 207; the fragment of SEQ ID NO:114 from about
 5 nucleotide 433 to about nucleotide 477; the fragment of SEQ ID NO:115 from about nucleotide 597 to about nucleotide 641; the fragment of SEQ ID NO:116 from about nucleotide 111 to about nucleotide 146; the fragment of SEQ ID NO:117 from about nucleotide 217 to about nucleotide 261; the fragment of SEQ ID NO:118 from about nucleotide 867 to about nucleotide 911; the fragment of SEQ ID NO:119 from about nucleotide 1082 to about nucleotide 1126; the fragment
 10 of SEQ ID NO:120 from about nucleotide 702 to about nucleotide 748; the fragment of SEQ ID NO:121 from about nucleotide 380 to about nucleotide 424; the fragment of SEQ ID NO:122 from about nucleotide 352 to about nucleotide 396; the fragment of SEQ ID NO:123 from about nucleotide 219 to about nucleotide 263; the fragment of SEQ ID NO:124 from about nucleotide 326 to about nucleotide 370; the fragment of SEQ ID NO:125 from about nucleotide 595 to about
 15 nucleotide 639; the fragment of SEQ ID NO:126 from about nucleotide 272 to about nucleotide 316; the fragment of SEQ ID NO:127 from about nucleotide 163 to about nucleotide 207; the fragment of SEQ ID NO:128 from about nucleotide 271 to about nucleotide 315; the fragment of SEQ ID NO:129 from about nucleotide 866 to about nucleotide 910; and the fragment of SEQ ID NO:130 from about nucleotide 487 to about nucleotide 531.

20 The invention also encompasses HTRM variants. A preferred HTRM variant is one which has at least about 80%, more preferably at least about 90%, and most preferably at least about 95% amino acid sequence identity to the HTRM amino acid sequence, and which contains at least one functional or structural characteristic of HTRM.

The invention also encompasses polynucleotides which encode HTRM. In a particular
 25 embodiment, the invention encompasses a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:66-130, which encodes HTRM.

The invention also encompasses a variant of a polynucleotide sequence encoding HTRM. In particular, such a variant polynucleotide sequence will have at least about 70%, more preferably at least about 85%, and most preferably at least about 95% polynucleotide sequence identity to the
 30 polynucleotide sequence encoding HTRM. A particular aspect of the invention encompasses a variant of a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:66-130 which has at least about 70%, more preferably at least about 85%, and most preferably at least about 95% polynucleotide sequence identity to a nucleic acid sequence selected from the
 35 group consisting of SEQ ID NO:66-130. Any one of the polynucleotide variants described above

can encode an amino acid sequence which contains at least one functional or structural characteristic of HTRM.

It will be appreciated by those skilled in the art that as a result of the degeneracy of the genetic code, a multitude of polynucleotide sequences encoding HTRM, some bearing minimal
5 similarity to the polynucleotide sequences of any known and naturally occurring gene, may be produced. Thus, the invention contemplates each and every possible variation of polynucleotide sequence that could be made by selecting combinations based on possible codon choices. These combinations are made in accordance with the standard triplet genetic code as applied to the polynucleotide sequence of naturally occurring HTRM, and all such variations are to be
10 considered as being specifically disclosed.

Although nucleotide sequences which encode HTRM and its variants are preferably capable of hybridizing to the nucleotide sequence of the naturally occurring HTRM under appropriately selected conditions of stringency, it may be advantageous to produce nucleotide sequences encoding HTRM or its derivatives possessing a substantially different codon usage,
15 e.g., inclusion of non-naturally occurring codons. Codons may be selected to increase the rate at which expression of the peptide occurs in a particular prokaryotic or eukaryotic host in accordance with the frequency with which particular codons are utilized by the host. Other reasons for substantially altering the nucleotide sequence encoding HTRM and its derivatives without altering the encoded amino acid sequences include the production of RNA transcripts having more
20 desirable properties, such as a greater half-life, than transcripts produced from the naturally occurring sequence.

The invention also encompasses production of DNA sequences which encode HTRM and HTRM derivatives, or fragments thereof, entirely by synthetic chemistry. After production, the synthetic sequence may be inserted into any of the many available expression vectors and cell
25 systems using reagents well known in the art. Moreover, synthetic chemistry may be used to introduce mutations into a sequence encoding HTRM or any fragment thereof.

Also encompassed by the invention are polynucleotide sequences that are capable of hybridizing to the claimed polynucleotide sequences, and, in particular, to those shown in SEQ ID NO:66-130 and fragments thereof under various conditions of stringency. (See, e.g., Wahl, G.M.
30 and S.L. Berger (1987) *Methods Enzymol.* 152:399-407; Kimmel, A.R. (1987) *Methods Enzymol.* 152:507-511.) For example, stringent salt concentration will ordinarily be less than about 750 mM NaCl and 75 mM trisodium citrate, preferably less than about 500 mM NaCl and 50 mM trisodium citrate, and most preferably less than about 250 mM NaCl and 25 mM trisodium citrate. Low stringency hybridization can be obtained in the absence of organic solvent, e.g., formamide, while
35 high stringency hybridization can be obtained in the presence of at least about 35% formamide.

and most preferably at least about 50% formamide. Stringent temperature conditions will ordinarily include temperatures of at least about 30°C, more preferably of at least about 37°C, and most preferably of at least about 42°C. Varying additional parameters, such as hybridization time, the concentration of detergent, e.g., sodium dodecyl sulfate (SDS), and the inclusion or exclusion
5 of carrier DNA, are well known to those skilled in the art. Various levels of stringency are accomplished by combining these various conditions as needed. In a preferred embodiment, hybridization will occur at 30°C in 750 mM NaCl, 75 mM trisodium citrate, and 1% SDS. In a more preferred embodiment, hybridization will occur at 37°C in 500 mM NaCl, 50 mM trisodium citrate, 1% SDS, 35% formamide, and 100 µg/ml denatured salmon sperm DNA (ssDNA). In a
10 most preferred embodiment, hybridization will occur at 42°C in 250 mM NaCl, 25 mM trisodium citrate, 1% SDS, 50 % formamide, and 200 µg/ml ssDNA. Useful variations on these conditions will be readily apparent to those skilled in the art.

The washing steps which follow hybridization can also vary in stringency. Wash stringency conditions can be defined by salt concentration and by temperature. As above, wash
15 stringency can be increased by decreasing salt concentration or by increasing temperature. For example, stringent salt concentration for the wash steps will preferably be less than about 30 mM NaCl and 3 mM trisodium citrate, and most preferably less than about 15 mM NaCl and 1.5 mM trisodium citrate. Stringent temperature conditions for the wash steps will ordinarily include temperature of at least about 25°C, more preferably of at least about 42°C, and most preferably of
20 at least about 68°C. In a preferred embodiment, wash steps will occur at 25°C in 30 mM NaCl, 3 mM trisodium citrate, and 0.1% SDS. In a more preferred embodiment, wash steps will occur at 42°C in 15 mM NaCl, 1.5 mM trisodium citrate, and 0.1% SDS. In a most preferred embodiment, wash steps will occur at 68°C in 15 mM NaCl, 1.5 mM trisodium citrate, and 0.1% SDS. Additional variations on these conditions will be readily apparent to those skilled in the art.

25 Methods for DNA sequencing are well known in the art and may be used to practice any of the embodiments of the invention. The methods may employ such enzymes as the Klenow fragment of DNA polymerase I, SEQUENASE (US Biochemical, Cleveland OH), Taq polymerase (Perkin-Elmer), thermostable T7 polymerase (Amersham Pharmacia Biotech, Piscataway NJ), or combinations of polymerases and proofreading exonucleases such as those found in the
30 ELONGASE amplification system (Life Technologies, Gaithersburg MD). Preferably, sequence preparation is automated with machines such as the Hamilton MICROLAB 2200 (Hamilton, Reno NV), Peltier Thermal Cycler 200 (PTC200; MJ Research, Watertown MA) and the ABI CATALYST 800 (Perkin-Elmer). Sequencing is then carried out using either ABI 373 or 377 DNA sequencing systems (Perkin-Elmer) or the MEGABACE 1000 DNA sequencing system
35 (Molecular Dynamics, Sunnyvale CA). The resulting sequences are analyzed using a variety of

algorithms which are well known in the art. (See, e.g., Ausubel, F.M. (1997) Short Protocols in Molecular Biology, John Wiley & Sons, New York NY, unit 7.7; Meyers, R.A. (1995) Molecular Biology and Biotechnology, Wiley VCH, New York NY, pp. 856-853.)

The nucleic acid sequences encoding HTRM may be extended utilizing a partial
5 nucleotide sequence and employing various PCR-based methods known in the art to detect upstream sequences, such as promoters and regulatory elements. For example, one method which may be employed, restriction-site PCR, uses universal and nested primers to amplify unknown sequence from genomic DNA within a cloning vector. (See, e.g., Sarkar, G. (1993) *PCR Methods Applic.* 2:318-322.) Another method, inverse PCR, uses primers that extend in divergent
10 directions to amplify unknown sequence from a circularized template. The template is derived from restriction fragments comprising a known genomic locus and surrounding sequences. (See, e.g., Triglia, T. et al. (1988) *Nucleic Acids Res.* 16:8186.) A third method, capture PCR, involves PCR amplification of DNA fragments adjacent to known sequences in human and yeast artificial chromosome DNA. (See, e.g., Lagerstrom, M. et al. (1991) *PCR Methods Applic.* 1:111-119.) In
15 this method, multiple restriction enzyme digestions and ligations may be used to insert an engineered double-stranded sequence into a region of unknown sequence before performing PCR. Other methods which may be used to retrieve unknown sequences are known in the art. (See, e.g., Parker, J.D. et al. (1991) *Nucleic Acids Res.* 19:3055-306). Additionally, one may use PCR, nested primers, and PROMOTERFINDER libraries (Clontech, Palo Alto CA) to walk genomic
20 DNA. This procedure avoids the need to screen libraries and is useful in finding intron/exon junctions. For all PCR-based methods, primers may be designed using commercially available software, such as OLIGO 4.06 Primer Analysis software (National Biosciences, Plymouth MN) or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the template at temperatures of about 68°C to 72°C.

25 When screening for full-length cDNAs, it is preferable to use libraries that have been size-selected to include larger cDNAs. In addition, random-primed libraries, which often include sequences containing the 5' regions of genes, are preferable for situations in which an oligo d(T) library does not yield a full-length cDNA. Genomic libraries may be useful for extension of sequence into 5' non-transcribed regulatory regions.

30 Capillary electrophoresis systems which are commercially available may be used to analyze the size or confirm the nucleotide sequence of sequencing or PCR products. In particular, capillary sequencing may employ flowable polymers for electrophoretic separation, four different nucleotide-specific, laser-stimulated fluorescent dyes, and a charge coupled device camera for detection of the emitted wavelengths. Output/light intensity may be converted to electrical signal
35 using appropriate software (e.g., GENOTYPER and SEQUENCE NAVIGATOR, Perkin-Elmer),

and the entire process from loading of samples to computer analysis and electronic data display may be computer controlled. Capillary electrophoresis is especially preferable for sequencing small DNA fragments which may be present in limited amounts in a particular sample.

In another embodiment of the invention, polynucleotide sequences or fragments thereof
5 which encode HTRM may be cloned in recombinant DNA molecules that direct expression of HTRM, or fragments or functional equivalents thereof, in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be produced and used to express HTRM.

10 The nucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter HTRM-encoding sequences for a variety of purposes including, but not limited to, modification of the cloning, processing, and/or expression of the gene product. DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. For example,
15 oligonucleotide-mediated site-directed mutagenesis may be used to introduce mutations that create new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, and so forth.

In another embodiment, sequences encoding HTRM may be synthesized, in whole or in part, using chemical methods well known in the art. (See, e.g., Caruthers, M.H. et al. (1980) Nucl.
20 Acids Res. Symp. Ser. 215-223, and Horn, T. et al. (1980) Nucl. Acids Res. Symp. Ser. 225-232.) Alternatively, HTRM itself or a fragment thereof may be synthesized using chemical methods. For example, peptide synthesis can be performed using various solid-phase techniques. (See, e.g., Roberge, J.Y. et al. (1995) Science 269:202-204.) Automated synthesis may be achieved using the ABI 431A Peptide Synthesizer (Perkin-Elmer). Additionally, the amino acid sequence of
25 HTRM, or any part thereof, may be altered during direct synthesis and/or combined with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

The peptide may be substantially purified by preparative high performance liquid chromatography. (See, e.g., Chiez, R.M. and F.Z. Regnier (1990) Methods Enzymol. 182:392-421.) The composition of the synthetic peptides may be confirmed by amino acid analysis or by
30 sequencing. (See, e.g., Creighton, T. (1984) Proteins. Structures and Molecular Properties, WH Freeman, New York NY.)

In order to express a biologically active HTRM, the nucleotide sequences encoding HTRM or derivatives thereof may be inserted into an appropriate expression vector, i.e., a vector which contains the necessary elements for transcriptional and translational control of the inserted
35 coding sequence in a suitable host. These elements include regulatory sequences, such as

enhancers, constitutive and inducible promoters, and 5' and 3' untranslated regions in the vector and in polynucleotide sequences encoding HTRM. Such elements may vary in their strength and specificity. Specific initiation signals may also be used to achieve more efficient translation of sequences encoding HTRM. Such signals include the ATG initiation codon and adjacent
5 sequences, e.g. the Kozak sequence. In cases where sequences encoding HTRM and its initiation codon and upstream regulatory sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a fragment thereof, is inserted, exogenous translational control signals including an in-frame ATG initiation codon should be provided by the vector. Exogenous
10 translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers appropriate for the particular host cell system used. (See, e.g., Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162.)

Methods which are well known to those skilled in the art may be used to construct
15 expression vectors containing sequences encoding HTRM and appropriate transcriptional and translational control elements. These methods include in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. (See, e.g., Sambrook, J. et al. (1989) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview NY, ch. 4, 8, and 16-17; Ausubel, F.M. et al. (1995) Current Protocols in Molecular Biology, John Wiley & Sons,
20 New York NY, ch. 9, 13, and 16.)

A variety of expression vector/host systems may be utilized to contain and express sequences encoding HTRM. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with viral
25 expression vectors (e.g., baculovirus); plant cell systems transformed with viral expression vectors (e.g., cauliflower mosaic virus, CaMV, or tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems. The invention is not limited by the host cell employed.

In bacterial systems, a number of cloning and expression vectors may be selected
30 depending upon the use intended for polynucleotide sequences encoding HTRM. For example, routine cloning, subcloning, and propagation of polynucleotide sequences encoding HTRM can be achieved using a multifunctional E. coli vector such as PBLUESCRIPT (Stratagene, La Jolla CA) or pSPORT1 plasmid (Life Technologies). Ligation of sequences encoding HTRM into the vector's multiple cloning site disrupts the *lacZ* gene, allowing a colorimetric screening procedure
35 for identification of transformed bacteria containing recombinant molecules. In addition, these

vectors may be useful for in vitro transcription, dideoxy sequencing, single strand rescue with helper phage, and creation of nested deletions in the cloned sequence. (See, e.g., Van Heeke, G. and S.M. Schuster (1989) J. Biol. Chem. 264:5503-5509.) When large quantities of HTRM are needed, e.g. for the production of antibodies, vectors which direct high level expression of HTRM
5 may be used. For example, vectors containing the strong, inducible T5 or T7 bacteriophage promoter may be used.

Yeast expression systems may be used for production of HTRM. A number of vectors containing constitutive or inducible promoters, such as alpha factor, alcohol oxidase, and PGH, may be used in the yeast Saccharomyces cerevisiae or Pichia pastoris. In addition, such vectors
10 direct either the secretion or intracellular retention of expressed proteins and enable integration of foreign sequences into the host genome for stable propagation. (See, e.g., Ausubel, 1995, supra; Grant et al. (1987) Methods Enzymol. 153:516-54; and Scorer, C. A. et al. (1994) Bio/Technology 12:181-184.)

Plant systems may also be used for expression of HTRM. Transcription of sequences
15 encoding HTRM may be driven viral promoters, e.g., the 35S and 19S promoters of CaMV used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) EMBO J. 6:307-311). Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used. (See, e.g., Coruzzi, G. et al. (1984) EMBO J. 3:1671-1680; Broglie, R. et al. (1984) Science 224:838-843; and Winter, J. et al. (1991) Results Probl. Cell
20 Differ. 17:85-105.) These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. (See, e.g., The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196.)

In mammalian cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, sequences encoding HTRM may be ligated
25 into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain infective virus which expresses HTRM in host cells. (See, e.g., Logan, J. and T. Shenk (1984) Proc. Natl. Acad. Sci. 81:3655-3659.) In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.
30 SV40 or EBV-based vectors may also be used for high-level protein expression.

Human artificial chromosomes (HACs) may also be employed to deliver larger fragments of DNA than can be contained in and expressed from a plasmid. HACs of about 6 kb to 10 Mb are constructed and delivered via conventional delivery methods (liposomes, polycationic amino polymers, or vesicles) for therapeutic purposes. (See, e.g., Harrington, J.J. et al. (1997) Nat Genet.
35 15:345-355.)

For long term production of recombinant proteins in mammalian systems, stable expression of HTRM in cell lines is preferred. For example, sequences encoding HTRM can be transformed into cell lines using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate
5 vector. Following the introduction of the vector, cells may be allowed to grow for about 1 to 2 days in enriched media before being switched to selective media. The purpose of the selectable marker is to confer resistance to a selective agent, and its presence allows growth and recovery of cells which successfully express the introduced sequences. Resistant clones of stably transformed cells may be propagated using tissue culture techniques appropriate to the cell type.

10 Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase and adenine phosphoribosyltransferase genes, for use in *tk*⁻ or *apv*⁻ cells, respectively. (See, e.g., Wigler, M. et al. (1977) Cell 11:223-232; Lowy, I. et al. (1980) Cell 22:817-823.) Also, antimetabolite, antibiotic, or herbicide resistance can be used as the basis for selection. For example, *dhfr* confers
15 resistance to methotrexate; *neo* confers resistance to the aminoglycosides, neomycin and G-418; and *als* or *pat* confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively. (See, e.g., Wigler, M. et al. (1980) Proc. Natl. Acad. Sci. 77:3567-3570; Colbere-Garapin, F. et al. (1981) J. Mol. Biol. 150:1-14.) Additional selectable genes have been described, e.g., *trpB* and *hisD*, which alter cellular requirements for metabolites. (See, e.g.,
20 Hartman, S.C. and R.C. Mulligan (1988) Proc. Natl. Acad. Sci. 85:8047-8051.) Visible markers, e.g., anthocyanins, green fluorescent proteins (GFP; Clontech), β glucuronidase and its substrate β -glucuronide, or luciferase and its substrate luciferin may be used. These markers can be used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system. (See, e.g., Rhodes, C.A. (1995) Methods Mol.
25 Biol. 55:121-131.)

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, the presence and expression of the gene may need to be confirmed. For example, if the sequence encoding HTRM is inserted within a marker gene sequence, transformed cells containing sequences encoding HTRM can be identified by the absence of marker gene
30 function. Alternatively, a marker gene can be placed in tandem with a sequence encoding HTRM under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

In general, host cells that contain the nucleic acid sequence encoding HTRM and that express HTRM may be identified by a variety of procedures known to those of skill in the art.
35 These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations, PCR

amplification, and protein bioassay or immunoassay techniques which include membrane solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein sequences.

Immunological methods for detecting and measuring the expression of HTRM using either
5 specific polyclonal or monoclonal antibodies are known in the art. Examples of such techniques include enzyme-linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on HTRM is preferred, but a competitive binding assay may be employed. These and other assays are well known in the art.
10 (See, e.g., Hampton, R. et al. (1990) Serological Methods, a Laboratory Manual, APS Press, St Paul MN. Sect. IV; Coligan, J. E. et al. (1997) Current Protocols in Immunology, Greene Pub. Associates and Wiley-Interscience, New York NY; and Pound, J.D. (1998) Immunochemical Protocols, Humana Press. Totowa NJ).

A wide variety of labels and conjugation techniques are known by those skilled in the art
15 and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides encoding HTRM include oligolabeling, nick translation, end-labeling, or PCR amplification using a labeled nucleotide. Alternatively, the sequences encoding HTRM, or any fragments thereof, may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are
20 commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits, such as those provided by Amersham Pharmacia Biotech, Promega (Madison WI), and US Biochemical. Suitable reporter molecules or labels which may be used for ease of detection include radionuclides, enzymes,
25 fluorescent, chemiluminescent, or chromogenic agents, as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with nucleotide sequences encoding HTRM may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a transformed cell may be secreted or retained intracellularly depending on the
30 sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides which encode HTRM may be designed to contain signal sequences which direct secretion of HTRM through a prokaryotic or eukaryotic cell membrane.

In addition, a host cell strain may be chosen for its ability to modulate expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications
35 of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation.

phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to specify protein targeting, folding, and/or activity.

Different host cells which have specific cellular machinery and characteristic mechanisms for post-translational activities (e.g., CHO, HeLa, MDCK, HEK293, and W138), are available from
5 the American Type Culture Collection (ATCC, Bethesda MD) and may be chosen to ensure the correct modification and processing of the foreign protein.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences encoding HTRM may be ligated to a heterologous sequence resulting in translation of a fusion protein in any of the aforementioned host systems. For example, a chimeric HTRM protein
10 containing a heterologous moiety that can be recognized by a commercially available antibody may facilitate the screening of peptide libraries for inhibitors of HTRM activity. Heterologous protein and peptide moieties may also facilitate purification of fusion proteins using commercially available affinity matrices. Such moieties include, but are not limited to, glutathione S-transferase (GST), maltose binding protein (MBP), thioredoxin (Trx), calmodulin binding peptide (CBP), 6-
15 His, FLAG, *c-myc*, and hemagglutinin (HA). GST, MBP, Trx, CBP, and 6-His enable purification of their cognate fusion proteins on immobilized glutathione, maltose, phenylarsine oxide, calmodulin, and metal-chelate resins, respectively. FLAG, *c-myc*, and hemagglutinin (HA) enable immunoaffinity purification of fusion proteins using commercially available monoclonal and polyclonal antibodies that specifically recognize these epitope tags. A fusion protein may also be
20 engineered to contain a proteolytic cleavage site located between the HTRM encoding sequence and the heterologous protein sequence, so that HTRM may be cleaved away from the heterologous moiety following purification. Methods for fusion protein expression and purification are discussed in Ausubel (1995, supra, ch 10). A variety of commercially available kits may also be used to facilitate expression and purification of fusion proteins.

25 In a further embodiment of the invention, synthesis of radiolabeled HTRM may be achieved in vitro using the TNT rabbit reticulocyte lysate or wheat germ extract systems (Promega). These systems couple transcription and translation of protein-coding sequences operably associated with the T7, T3, or SP6 promoters. Translation takes place in the presence of a radiolabeled amino acid precursor, preferably ³⁵S-methionine.

30 Fragments of HTRM may be produced not only by recombinant production, but also by direct peptide synthesis using solid-phase techniques. (See, e.g., Creighton, supra, pp. 55-60.) Protein synthesis may be performed by manual techniques or by automation. Automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin-Elmer). Various fragments of HTRM may be synthesized separately and then combined to produce the full length
35 molecule.

THERAPEUTICS

Chemical and structural similarity, e.g., in the context of sequences and motifs, exists between regions of HTRM and human transcriptional regulator molecules. In addition, the expression of HTRM is closely associated with cell proliferation, inflammation, and the immune response. Therefore, HTRM appears to play a role in cell proliferative and immune disorders. In the treatment of disorders associated with increased HTRM expression or activity, it is desirable to decrease the expression or activity of HTRM. In the treatment of disorders associated with decreased HTRM expression or activity, it is desirable to increase the expression or activity of HTRM.

Therefore, in one embodiment, HTRM or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HTRM. Examples of such disorders include, but are not limited to, a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia; cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; and an immune disorder such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma

In another embodiment, a vector capable of expressing HTRM or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HTRM including, but not limited to, those described above.

In a further embodiment, a pharmaceutical composition comprising a substantially purified HTRM in conjunction with a suitable pharmaceutical carrier may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HTRM including, but not limited to, those provided above.

5 In still another embodiment, an agonist which modulates the activity of HTRM may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HTRM including, but not limited to, those listed above.

In a further embodiment, an antagonist of HTRM may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of HTRM. Examples of
10 such disorders include, but are not limited to, those described above. In one aspect, an antibody which specifically binds HTRM may be used directly as an antagonist or indirectly as a targeting or delivery mechanism for bringing a pharmaceutical agent to cells or tissue which express HTRM.

In an additional embodiment, a vector expressing the complement of the polynucleotide
15 encoding HTRM may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of HTRM including, but not limited to, those described above.

In other embodiments, any of the proteins, antagonists, antibodies, agonists, complementary sequences, or vectors of the invention may be administered in combination with other appropriate therapeutic agents. Selection of the appropriate agents for use in combination
20 therapy may be made by one of ordinary skill in the art, according to conventional pharmaceutical principles. The combination of therapeutic agents may act synergistically to effect the treatment or prevention of the various disorders described above. Using this approach, one may be able to achieve therapeutic efficacy with lower dosages of each agent, thus reducing the potential for adverse side effects.

25 An antagonist of HTRM may be produced using methods which are generally known in the art. In particular, purified HTRM may be used to produce antibodies or to screen libraries of pharmaceutical agents to identify those which specifically bind HTRM. Antibodies to HTRM may also be generated using methods that are well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, and single chain antibodies, Fab fragments,
30 and fragments produced by a Fab expression library. Neutralizing antibodies (i.e., those which inhibit dimer formation) are especially preferred for therapeutic use.

For the production of antibodies, various hosts including goats, rabbits, rats, mice, humans, and others may be immunized by injection with HTRM or with any fragment or oligopeptide thereof which has immunogenic properties. Depending on the host species, various
35 adjuvants may be used to increase immunological response. Such adjuvants include, but are not

limited to. Freund's. mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, KLH, and dinitrophenol. Among adjuvants used in humans, BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are especially preferable.

5 It is preferred that the oligopeptides, peptides, or fragments used to induce antibodies to HTRM have an amino acid sequence consisting of at least about 5 amino acids, and, more preferably, of at least about 10 amino acids. It is also preferable that these oligopeptides, peptides, or fragments are identical to a portion of the amino acid sequence of the natural protein and contain the entire amino acid sequence of a small, naturally occurring molecule. Short stretches of
10 HTRM amino acids may be fused with those of another protein, such as KLH, and antibodies to the chimeric molecule may be produced.

Monoclonal antibodies to HTRM may be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique, the human B-cell hybridoma technique, and the EBV-
15 hybridoma technique. (See, e.g., Kohler, G. et al. (1975) Nature 256:495-497; Kozbor, D. et al. (1985) J. Immunol. Methods 81:31-42; Cote, R.J. et al. (1983) Proc. Natl. Acad. Sci. 80:2026-2030; and Cole, S.P. et al. (1984) Mol. Cell Biol. 62:109-120.)

In addition, techniques developed for the production of "chimeric antibodies," such as the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate
20 antigen specificity and biological activity, can be used. (See, e.g., Morrison, S.L. et al. (1984) Proc. Natl. Acad. Sci. 81:6851-6855; Neuberger, M.S. et al. (1984) Nature 312:604-608; and Takeda, S. et al. (1985) Nature 314:452-454.) Alternatively, techniques described for the production of single chain antibodies may be adapted, using methods known in the art, to produce HTRM-specific single chain antibodies. Antibodies with related specificity, but of distinct
25 idiotypic composition, may be generated by chain shuffling from random combinatorial immunoglobulin libraries. (See, e.g., Burton D.R. (1991) Proc. Natl. Acad. Sci. 88:10134-10137.)

Antibodies may also be produced by inducing in vivo production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents as disclosed in the literature. (See, e.g., Orlandi, R. et al. (1989) Proc. Natl. Acad. Sci. 86:
30 3833-3837; Winter, G. et al. (1991) Nature 349:293-299.)

Antibody fragments which contain specific binding sites for HTRM may also be generated. For example, such fragments include, but are not limited to, F(ab')₂ fragments produced by pepsin digestion of the antibody molecule and Fab fragments generated by reducing the disulfide bridges of the F(ab')₂ fragments. Alternatively, Fab expression libraries may be
35 constructed to allow rapid and easy identification of monoclonal Fab fragments with the desired

specificity. (See, e.g., Huse, W.D. et al. (1989) Science 246:1275-1281.)

Various immunoassays may be used for screening to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the measurement of complex formation between HTRM and its specific antibody. A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering HTRM epitopes is preferred, but a competitive binding assay may also be employed (Pound, supra).

Various methods such as Scatchard analysis in conjunction with radioimmunoassay techniques may be used to assess the affinity of antibodies for HTRM. Affinity is expressed as an association constant, K_a , which is defined as the molar concentration of HTRM-antibody complex divided by the molar concentrations of free antigen and free antibody under equilibrium conditions. The K_a determined for a preparation of polyclonal antibodies, which are heterogeneous in their affinities for multiple HTRM epitopes, represents the average affinity, or avidity, of the antibodies for HTRM. The K_a determined for a preparation of monoclonal antibodies, which are monospecific for a particular HTRM epitope, represents a true measure of affinity. High-affinity antibody preparations with K_a ranging from about 10^9 to 10^{12} L/mole are preferred for use in immunoassays in which the HTRM-antibody complex must withstand rigorous manipulations. Low-affinity antibody preparations with K_a ranging from about 10^6 to 10^7 L/mole are preferred for use in immunopurification and similar procedures which ultimately require dissociation of HTRM, preferably in active form, from the antibody (Catty, D. (1988) Antibodies, Volume I: A Practical Approach, IRL Press, Washington, DC; Liddell, J. E. and Cryer, A. (1991) A Practical Guide to Monoclonal Antibodies, John Wiley & Sons, New York NY).

The titer and avidity of polyclonal antibody preparations may be further evaluated to determine the quality and suitability of such preparations for certain downstream applications. For example, a polyclonal antibody preparation containing at least 1-2 mg specific antibody/ml, preferably 5-10 mg specific antibody/ml, is preferred for use in procedures requiring precipitation of HTRM-antibody complexes. Procedures for evaluating antibody specificity, titer, and avidity, and guidelines for antibody quality and usage in various applications, are generally available. (See, e.g., Catty, supra, and Coligan et al. supra.)

In another embodiment of the invention, the polynucleotides encoding HTRM, or any fragment or complement thereof, may be used for therapeutic purposes. In one aspect, the complement of the polynucleotide encoding HTRM may be used in situations in which it would be desirable to block the transcription of the mRNA. In particular, cells may be transformed with sequences complementary to polynucleotides encoding HTRM. Thus, complementary molecules

or fragments may be used to modulate HTRM activity, or to achieve regulation of gene function. Such technology is now well known in the art, and sense or antisense oligonucleotides or larger fragments can be designed from various locations along the coding or control regions of sequences encoding HTRM.

5 Expression vectors derived from retroviruses, adenoviruses, or herpes or vaccinia viruses, or from various bacterial plasmids, may be used for delivery of nucleotide sequences to the targeted organ, tissue, or cell population. Methods which are well known to those skilled in the art can be used to construct vectors to express nucleic acid sequences complementary to the polynucleotides encoding HTRM. (See, e.g., Sambrook, supra; Ausubel, 1995, supra.)

10 Genes encoding HTRM can be turned off by transforming a cell or tissue with expression vectors which express high levels of a polynucleotide, or fragment thereof, encoding HTRM. Such constructs may be used to introduce untranslatable sense or antisense sequences into a cell. Even in the absence of integration into the DNA, such vectors may continue to transcribe RNA molecules until they are disabled by endogenous nucleases. Transient expression may last for a
15 month or more with a non-replicating vector, and may last even longer if appropriate replication elements are part of the vector system.

As mentioned above, modifications of gene expression can be obtained by designing complementary sequences or antisense molecules (DNA, RNA, or PNA) to the control, 5', or regulatory regions of the gene encoding HTRM. Oligonucleotides derived from the transcription
20 initiation site, e.g., between about positions -10 and +10 from the start site, are preferred. Similarly, inhibition can be achieved using triple helix base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or regulatory molecules. Recent therapeutic advances using triplex DNA have been described in the literature. (See, e.g., Gee, J.E. et al.
25 (1994) in Huber, B.E. and B.I. Carr, Molecular and Immunologic Approaches, Futura Publishing, Mt. Kisco NY, pp. 163-177.) A complementary sequence or antisense molecule may also be designed to block translation of mRNA by preventing the transcript from binding to ribosomes.

Ribozymes, enzymatic RNA molecules, may also be used to catalyze the specific cleavage of RNA. The mechanism of ribozyme action involves sequence-specific hybridization of the
30 ribozyme molecule to complementary target RNA, followed by endonucleolytic cleavage. For example, engineered hammerhead motif ribozyme molecules may specifically and efficiently catalyze endonucleolytic cleavage of sequences encoding HTRM.

Specific ribozyme cleavage sites within any potential RNA target are initially identified by scanning the target molecule for ribozyme cleavage sites, including the following sequences:
35 GUA, GUU, and GUC. Once identified, short RNA sequences of between 15 and 20

ribonucleotides, corresponding to the region of the target gene containing the cleavage site, may be evaluated for secondary structural features which may render the oligonucleotide inoperable. The suitability of candidate targets may also be evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays.

5 Complementary ribonucleic acid molecules and ribozymes of the invention may be prepared by any method known in the art for the synthesis of nucleic acid molecules. These include techniques for chemically synthesizing oligonucleotides such as solid phase phosphoramidite chemical synthesis. Alternatively, RNA molecules may be generated by in vitro and in vivo transcription of DNA sequences encoding HTRM. Such DNA sequences may be
10 incorporated into a wide variety of vectors with suitable RNA polymerase promoters such as T7 or SP6. Alternatively, these cDNA constructs that synthesize complementary RNA, constitutively or inducibly, can be introduced into cell lines, cells, or tissues.

RNA molecules may be modified to increase intracellular stability and half-life. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'
15 ends of the molecule, or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the backbone of the molecule. This concept is inherent in the production of PNAs and can be extended in all of these molecules by the inclusion of nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, cytidine, guanine, thymine, and uridine which are not as easily recognized by
20 endogenous endonucleases.

Many methods for introducing vectors into cells or tissues are available and equally suitable for use in vivo, in vitro, and ex vivo. For ex vivo therapy, vectors may be introduced into stem cells taken from the patient and clonally propagated for autologous transplant back into that same patient. Delivery by transfection, by liposome injections, or by polycationic amino polymers
25 may be achieved using methods which are well known in the art. (See, e.g., Goldman, C.K. et al. (1997) Nature Biotechnology 15:462-466.)

Any of the therapeutic methods described above may be applied to any subject in need of such therapy, including, for example, mammals such as dogs, cats, cows, horses, rabbits, monkeys, and most preferably, humans.

30 An additional embodiment of the invention relates to the administration of a pharmaceutical or sterile composition, in conjunction with a pharmaceutically acceptable carrier, for any of the therapeutic effects discussed above. Such pharmaceutical compositions may consist of HTRM, antibodies to HTRM, and mimetics, agonists, antagonists, or inhibitors of HTRM. The compositions may be administered alone or in combination with at least one other agent, such as a
35 stabilizing compound, which may be administered in any sterile, biocompatible pharmaceutical

carrier including, but not limited to, saline, buffered saline, dextrose, and water. The compositions may be administered to a patient alone, or in combination with other agents, drugs, or hormones.

The pharmaceutical compositions utilized in this invention may be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intra-arterial, 5 intramedullary, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, or rectal means.

In addition to the active ingredients, these pharmaceutical compositions may contain suitable pharmaceutically-acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used 10 pharmaceutically. Further details on techniques for formulation and administration may be found in the latest edition of Remington's Pharmaceutical Sciences (Maack Publishing, Easton PA).

Pharmaceutical compositions for oral administration can be formulated using pharmaceutically acceptable carriers well known in the art in dosages suitable for oral administration. Such carriers enable the pharmaceutical compositions to be formulated as tablets, 15 pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions, and the like, for ingestion by the patient.

Pharmaceutical preparations for oral use can be obtained through combining active compounds with solid excipient and processing the resultant mixture of granules (optionally, after grinding) to obtain tablets or dragee cores. Suitable auxiliaries can be added, if desired. Suitable 20 excipients include carbohydrate or protein fillers, such as sugars, including lactose, sucrose, mannitol, and sorbitol; starch from corn, wheat, rice, potato, or other plants; cellulose, such as methyl cellulose, hydroxypropylmethyl-cellulose, or sodium carboxymethylcellulose; gums, including arabic and tragacanth; and proteins, such as gelatin and collagen. If desired, disintegrating or solubilizing agents may be added, such as the cross-linked polyvinyl pyrrolidone, 25 agar, and alginic acid or a salt thereof, such as sodium alginate.

Dragee cores may be used in conjunction with suitable coatings, such as concentrated sugar solutions, which may also contain gum arabic, talc, polyvinylpyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for 30 product identification or to characterize the quantity of active compound, i.e., dosage.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a coating, such as glycerol or sorbitol. Push-fit capsules can contain active ingredients mixed with fillers or binders, such as lactose or starches, lubricants, such as talc or magnesium stearate, and, optionally, stabilizers. In soft 35 capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty

oils, liquid, or liquid polyethylene glycol with or without stabilizers.

Pharmaceutical formulations suitable for parenteral administration may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, Ringer's solution, or physiologically buffered saline. Aqueous injection suspensions may contain
5 substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils, such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate, triglycerides, or liposomes. Non-lipid polycationic amino polymers may also be used for delivery. Optionally, the
10 suspension may also contain suitable stabilizers or agents to increase the solubility of the compounds and allow for the preparation of highly concentrated solutions.

For topical or nasal administration, penetrants appropriate to the particular barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

The pharmaceutical compositions of the present invention may be manufactured in a
15 manner that is known in the art, e.g., by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, or lyophilizing processes.

The pharmaceutical composition may be provided as a salt and can be formed with many acids, including but not limited to, hydrochloric, sulfuric, acetic, lactic, tartaric, malic, and succinic acid. Salts tend to be more soluble in aqueous or other protonic solvents than are the
20 corresponding free base forms. In other cases, the preferred preparation may be a lyophilized powder which may contain any or all of the following: 1 mM to 50 mM histidine, 0.1% to 2% sucrose, and 2% to 7% mannitol, at a pH range of 4.5 to 5.5, that is combined with buffer prior to use.

After pharmaceutical compositions have been prepared, they can be placed in an
25 appropriate container and labeled for treatment of an indicated condition. For administration of HTRM, such labeling would include amount, frequency, and method of administration.

Pharmaceutical compositions suitable for use in the invention include compositions wherein the active ingredients are contained in an effective amount to achieve the intended purpose. The determination of an effective dose is well within the capability of those skilled in the
30 art.

For any compound, the therapeutically effective dose can be estimated initially either in cell culture assays, e.g., of neoplastic cells or in animal models such as mice, rats, rabbits, dogs, or
pigs. An animal model may also be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes
35 for administration in humans.

A therapeutically effective dose refers to that amount of active ingredient, for example HTRM or fragments thereof, antibodies of HTRM, and agonists, antagonists or inhibitors of HTRM, which ameliorates the symptoms or condition. Therapeutic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or with experimental animals, such as by calculating the ED_{50} (the dose therapeutically effective in 50% of the population) or LD_{50} (the dose lethal to 50% of the population) statistics. The dose ratio of toxic to therapeutic effects is the therapeutic index, and it can be expressed as the LD_{50}/ED_{50} ratio. Pharmaceutical compositions which exhibit large therapeutic indices are preferred. The data obtained from cell culture assays and animal studies are used to formulate a range of dosage for human use. The dosage contained in such compositions is preferably within a range of circulating concentrations that includes the ED_{50} with little or no toxicity. The dosage varies within this range depending upon the dosage form employed, the sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors related to the subject requiring treatment. Dosage and administration are adjusted to provide sufficient levels of the active moiety or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, the general health of the subject, the age, weight, and gender of the subject, time and frequency of administration, drug combination(s), reaction sensitivities, and response to therapy. Long-acting pharmaceutical compositions may be administered every 3 to 4 days, every week, or biweekly depending on the half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from about $0.1 \mu\text{g}$ to $100,000 \mu\text{g}$, up to a total dose of about 1 gram, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art. Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

DIAGNOSTICS

In another embodiment, antibodies which specifically bind HTRM may be used for the diagnosis of disorders characterized by expression of HTRM, or in assays to monitor patients being treated with HTRM or agonists, antagonists, or inhibitors of HTRM. Antibodies useful for diagnostic purposes may be prepared in the same manner as described above for therapeutics. Diagnostic assays for HTRM include methods which utilize the antibody and a label to detect HTRM in human body fluids or in extracts of cells or tissues. The antibodies may be used with or without modification, and may be labeled by covalent or non-covalent attachment of a reporter molecule. A wide variety of reporter molecules, several of which are described above, are known

in the art and may be used.

A variety of protocols for measuring HTRM, including ELISAs, RIAs, and FACS, are known in the art and provide a basis for diagnosing altered or abnormal levels of HTRM expression. Normal or standard values for HTRM expression are established by combining body fluids or cell extracts taken from normal mammalian subjects, preferably human, with antibody to HTRM under conditions suitable for complex formation. The amount of standard complex formation may be quantitated by various methods, preferably by photometric means. Quantities of HTRM expressed in subject, control, and disease samples from biopsied tissues are compared with the standard values. Deviation between standard and subject values establishes the parameters for diagnosing disease.

In another embodiment of the invention, the polynucleotides encoding HTRM may be used for diagnostic purposes. The polynucleotides which may be used include oligonucleotide sequences, complementary RNA and DNA molecules, and PNAs. The polynucleotides may be used to detect and quantitate gene expression in biopsied tissues in which expression of HTRM may be correlated with disease. The diagnostic assay may be used to determine absence, presence, and excess expression of HTRM, and to monitor regulation of HTRM levels during therapeutic intervention.

In one aspect, hybridization with PCR probes which are capable of detecting polynucleotide sequences, including genomic sequences, encoding HTRM or closely related molecules may be used to identify nucleic acid sequences which encode HTRM. The specificity of the probe, whether it is made from a highly specific region, e.g., the 5' regulatory region, or from a less specific region, e.g., a conserved motif, and the stringency of the hybridization or amplification (maximal, high, intermediate, or low), will determine whether the probe identifies only naturally occurring sequences encoding HTRM, allelic variants, or related sequences.

Probes may also be used for the detection of related sequences, and should preferably have at least 50% sequence identity to any of the HTRM encoding sequences. The hybridization probes of the subject invention may be DNA or RNA and may be derived from the sequence of SEQ ID NO:66-130 or from genomic sequences including promoters, enhancers, and introns of the HTRM gene.

Means for producing specific hybridization probes for DNAs encoding HTRM include the cloning of polynucleotide sequences encoding HTRM or HTRM derivatives into vectors for the production of mRNA probes. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes *in vitro* by means of the addition of the appropriate RNA polymerases and the appropriate labeled nucleotides. Hybridization probes may be labeled by a variety of reporter groups, for example, by radionuclides such as ^{32}P or ^{35}S , or by enzymatic labels.

such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems, and the like.

Polynucleotide sequences encoding HTRM may be used for the diagnosis of disorders associated with expression of HTRM. Examples of such disorders include, but are not limited to, a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia; cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; and an immune disorder such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma. The polynucleotide sequences encoding HTRM may be used in Southern or northern analysis, dot blot, or other membrane-based technologies; in PCR technologies; in dipstick, pin, and multiformat ELISA-like assays; and in microarrays utilizing fluids or tissues from patients to detect altered HTRM expression. Such qualitative or quantitative methods are well known in the art.

In a particular aspect, the nucleotide sequences encoding HTRM may be useful in assays that detect the presence of associated disorders, particularly those mentioned above. The nucleotide sequences encoding HTRM may be labeled by standard methods and added to a fluid or tissue sample from a patient under conditions suitable for the formation of hybridization complexes. After a suitable incubation period, the sample is washed and the signal is quantitated and compared with a standard value. If the amount of signal in the patient sample is significantly altered in comparison to a control sample then the presence of altered levels of nucleotide sequences encoding HTRM in the sample indicates the presence of the associated disorder. Such

assays may also be used to evaluate the efficacy of a particular therapeutic treatment regimen in animal studies, in clinical trials, or to monitor the treatment of an individual patient.

In order to provide a basis for the diagnosis of a disorder associated with expression of HTRM, a normal or standard profile for expression is established. This may be accomplished by
5 combining body fluids or cell extracts taken from normal subjects, either animal or human, with a sequence, or a fragment thereof, encoding HTRM, under conditions suitable for hybridization or amplification. Standard hybridization may be quantified by comparing the values obtained from normal subjects with values from an experiment in which a known amount of a substantially purified polynucleotide is used. Standard values obtained in this manner may be compared with
10 values obtained from samples from patients who are symptomatic for a disorder. Deviation from standard values is used to establish the presence of a disorder.

Once the presence of a disorder is established and a treatment protocol is initiated, hybridization assays may be repeated on a regular basis to determine if the level of expression in the patient begins to approximate that which is observed in the normal subject. The results
15 obtained from successive assays may be used to show the efficacy of treatment over a period ranging from several days to months.

With respect to cancer, the presence of an abnormal amount of transcript (either under- or overexpressed) in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the
20 appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

Additional diagnostic uses for oligonucleotides designed from the sequences encoding HTRM may involve the use of PCR. These oligomers may be chemically synthesized, generated
25 enzymatically, or produced *in vitro*. Oligomers will preferably contain a fragment of a polynucleotide encoding HTRM, or a fragment of a polynucleotide complementary to the polynucleotide encoding HTRM, and will be employed under optimized conditions for identification of a specific gene or condition. Oligomers may also be employed under less stringent conditions for detection or quantitation of closely related DNA or RNA sequences.

30 Methods which may also be used to quantitate the expression of HTRM include radiolabeling or biotinylating nucleotides, coamplification of a control nucleic acid, and interpolating results from standard curves. (See, e.g., Melby, P.C. et al. (1993) J. Immunol. Methods 159:235-244; Duplaa, C. et al. (1993) Anal. Biochem. 229-236.) The speed of quantitation of multiple samples may be accelerated by running the assay in an ELISA format
35 where the oligomer of interest is presented in various dilutions and a spectrophotometric or

colorimetric response gives rapid quantitation.

In further embodiments, oligonucleotides or longer fragments derived from any of the polynucleotide sequences described herein may be used as targets in a microarray. The microarray can be used to monitor the expression level of large numbers of genes simultaneously
5 and to identify genetic variants, mutations, and polymorphisms. This information may be used to determine gene function, to understand the genetic basis of a disorder, to diagnose a disorder, and to develop and monitor the activities of therapeutic agents.

Microarrays may be prepared, used, and analyzed using methods known in the art. (See, e.g., Brennan, T.M. et al. (1995) U.S. Patent No. 5,474,796; Schena, M. et al. (1996) Proc. Natl.
10 Acad. Sci. 93:10614-10619; Baldeschweiler et al. (1995) PCT application WO95/251116; Shalon, D. et al. (1995) PCT application WO95/35505; Heller, R.A. et al. (1997) Proc. Natl. Acad. Sci. 94:2150-2155; and Heller, M.J. et al. (1997) U.S. Patent No. 5,605,662.)

In another embodiment of the invention, nucleic acid sequences encoding HTRM may be used to generate hybridization probes useful in mapping the naturally occurring genomic
15 sequence. The sequences may be mapped to a particular chromosome, to a specific region of a chromosome, or to artificial chromosome constructions, e.g., human artificial chromosomes (HACs), yeast artificial chromosomes (YACs), bacterial artificial chromosomes (BACs), bacterial P1 constructions, or single chromosome cDNA libraries. (See, e.g., Harrington, J.J. et al. (1997) Nat Genet. 15:345-355; Price, C.M. (1993) Blood Rev. 7:127-134; and Trask, B.J. (1991) Trends
20 Genet. 7:149-154.)

Fluorescent in situ hybridization (FISH) may be correlated with other physical chromosome mapping techniques and genetic map data. (See, e.g., Heinz-Ulrich, et al. (1995) in Meyers, supra, pp. 965-968.) Examples of genetic map data can be found in various scientific journals or at the Online Mendelian Inheritance in Man (OMIM) site. Correlation between the
25 location of the gene encoding HTRM on a physical chromosomal map and a specific disorder, or a predisposition to a specific disorder, may help define the region of DNA associated with that disorder. The nucleotide sequences of the invention may be used to detect differences in gene sequences among normal, carrier, and affected individuals.

In situ hybridization of chromosomal preparations and physical mapping techniques, such
30 as linkage analysis using established chromosomal markers, may be used for extending genetic maps. Often the placement of a gene on the chromosome of another mammalian species, such as mouse, may reveal associated markers even if the number or arm of a particular human chromosome is not known. New sequences can be assigned to chromosomal arms by physical mapping. This provides valuable information to investigators searching for disease genes using
35 positional cloning or other gene discovery techniques. Once the disease or syndrome has been

crudely localized by genetic linkage to a particular genomic region, e.g., ataxia-telangiectasia to 11q22-23. any sequences mapping to that area may represent associated or regulatory genes for further investigation. (See, e.g., Gatti, R.A. et al. (1988) Nature 336:577-580.) The nucleotide sequence of the subject invention may also be used to detect differences in the chromosomal
5 location due to translocation, inversion, etc., among normal, carrier, or affected individuals.

In another embodiment of the invention, HTRM, its catalytic or immunogenic fragments, or oligopeptides thereof can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such screening may be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. The formation of
10 binding complexes between HTRM and the agent being tested may be measured.

Another technique for drug screening provides for high throughput screening of compounds having suitable binding affinity to the protein of interest. (See, e.g., Geysen, et al. (1984) PCT application WO84/03564.) In this method, large numbers of different small test compounds are synthesized on a solid substrate. The test compounds are reacted with HTRM, or
15 fragments thereof, and washed. Bound HTRM is then detected by methods well known in the art. Purified HTRM can also be coated directly onto plates for use in the aforementioned drug screening techniques. Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.

In another embodiment, one may use competitive drug screening assays in which
20 neutralizing antibodies capable of binding HTRM specifically compete with a test compound for binding HTRM. In this manner, antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with HTRM.

In additional embodiments, the nucleotide sequences which encode HTRM may be used in any molecular biology techniques that have yet to be developed, provided the new techniques rely
25 on properties of nucleotide sequences that are currently known, including, but not limited to, such properties as the triplet genetic code and specific base pair interactions.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of
30 the remainder of the disclosure in any way whatsoever.

The entire disclosure of all applications, patents, and publications, cited above and below, and of US provisional applications 60/084,254 (filed May 5, 1998), 60/095,827 (filed August 7, 1998), and 60/102,745 (filed Oct. 2, 1998) are hereby incorporated by reference.

EXAMPLES

35 I. Construction of cDNA Libraries

RNA was purchased from Clontech or isolated from tissues described in Table 4. Some tissues were homogenized and lysed in guanidinium isothiocyanate, while others were homogenized and lysed in phenol or in a suitable mixture of denaturants, such as TRIZOL (Life Technologies), a monophasic solution of phenol and guanidine isothiocyanate. The resulting lysates were centrifuged over CsCl cushions or extracted with chloroform. RNA was precipitated from the lysates with either isopropanol or sodium acetate and ethanol, or by other routine methods.

Phenol extraction and precipitation of RNA were repeated as necessary to increase RNA purity. In some cases, RNA was treated with DNase. For most libraries, poly(A⁺) RNA was isolated using oligo d(T)-coupled paramagnetic particles (Promega), OLIGOTEX latex particles (QIAGEN, Valencia CA), or an OLIGOTEX mRNA purification kit (QIAGEN). Alternatively, RNA was isolated directly from tissue lysates using other RNA isolation kits, e.g., the POLY(A)PURE mRNA purification kit (Ambion, Austin TX).

In some cases, Stratagene was provided with RNA and constructed the corresponding cDNA libraries. Otherwise, cDNA was synthesized and cDNA libraries were constructed with the UNIZAP vector system (Stratagene) or SUPERScript plasmid system (Life Technologies), using the recommended procedures or similar methods known in the art. (See, e.g., Ausubel, 1997, *supra*, units 5.1-6.6). Reverse transcription was initiated using oligo d(T) or random primers. Synthetic oligonucleotide adapters were ligated to double stranded cDNA, and the cDNA was digested with the appropriate restriction enzyme or enzymes. For most libraries, the cDNA was size-selected (300-1000 bp) using SEPHACRYL S1000, SEPHAROSE CL2B, or SEPHAROSE CL4B column chromatography (Amersham Pharmacia Biotech) or preparative agarose gel electrophoresis. cDNAs were ligated into compatible restriction enzyme sites of the polylinker of a suitable plasmid, e.g., PBLUESCRIPT plasmid (Stratagene), pSPORT1 plasmid (Life Technologies), or pINCY (Incyte Pharmaceuticals, Palo Alto CA). Recombinant plasmids were transformed into competent *E. coli* cells including XL1-Blue, XL1-BlueMRF, or SOLR from Stratagene or DH5 α , DH10B, or ElectroMAX DH10B from Life Technologies.

II. Isolation of cDNA Clones

Plasmids were recovered from host cells by *in vivo* excision, using the UNIZAP vector system (Stratagene) or cell lysis. Plasmids were purified using at least one of the following: a Magic or WIZARD Minipreps DNA purification system (Promega); an AGTC Miniprep purification kit (Edge Biosystems, Gaithersburg MD); and QIAWELL 8 Plasmid, QIAWELL 8 Plus Plasmid, QIAWELL 8 Ultra Plasmid purification systems or the REAL Prep 96 plasmid kit from QIAGEN. Following precipitation, plasmids were resuspended in 0.1 ml of distilled water and stored, with or without lyophilization, at 4°C.

Alternatively, a high-throughput method, such as the one described herein, can be used to screen a large number of samples.

5 fluorometric
fluorescence

III. Sequencing

The cDNAs were sequenced using a combination of the ABI PRISM 3100XL automated DNA sequencing system, calling software, a 1000 base pair primer, and a reaction kit.

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(DNASTAR).

using a search algorithm developed

670 sequence analysis system. In

Los Angeles, CA) was used to

determine how the sequence

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sequences containing regions of

sequences were scored with an initial value.

Subsequently, these homologous regions were examined using dot matrix homology plots to distinguish regions of homology from chance matches. Smith-Waterman alignments were used to display the results of the homology search.

Peptide and protein sequence homologies were ascertained using the INHERIT- 670
5 sequence analysis system using the methods similar to those used in DNA sequence homologies. Pattern Specification Language and parameter windows were used to search protein databases for sequences containing regions of homology which were scored with an initial value. Dot-matrix homology plots were examined to distinguish regions of significant homology from chance matches.

10 The polynucleotide sequences were validated by removing vector, linker, and polyA sequences and by masking ambiguous bases, using algorithms and programs based on BLAST, dynamic programming, and dinucleotide nearest neighbor analysis. The sequences were then queried against a selection of public databases such as GenBank primate, rodent, mammalian, vertebrate, and eukaryote databases, and BLOCKS to acquire annotation, using programs based on
15 BLAST, FASTA, and BLIMPS. The sequences were assembled into full length polynucleotide sequences using programs based on Phred, Phrap, and Consed, and were screened for open reading frames using programs based on GeneMark, BLAST, and FASTA. The full length polynucleotide sequences were translated to derive the corresponding full length amino acid sequences, and these full length sequences were subsequently analyzed by querying against
20 databases such as the GenBank databases (described above), SwissProt, BLOCKS, PRINTS, PFAM, and Prosite.

The programs described above for the assembly and analysis of full length polynucleotide and amino acid sequences were also used to identify polynucleotide sequence fragments from SEQ ID NO:110-130. Fragments from about 20 to about 4000 nucleotides which are useful in
25 hybridization and amplification technologies were described in The Invention section above.

IV. Northern Analysis

Northern analysis is a laboratory technique used to detect the presence of a transcript of a gene and involves the hybridization of a labeled nucleotide sequence to a membrane on which RNAs from a particular cell type or tissue have been bound. (See, e.g., Sambrook, supra, ch. 7;
30 Ausubel, 1995, supra, ch. 4 and 16.)

Analogous computer techniques applying BLAST were used to search for identical or related molecules in nucleotide databases such as GenBank or LIFESEQ database (Incyte Pharmaceuticals). This analysis is much faster than multiple membrane-based hybridizations. In addition, the sensitivity of the computer search can be modified to determine whether any
35 particular match is categorized as exact or similar. The basis of the search is the product score,

which is defined as:

$$\frac{\% \text{ sequence identity} \times \% \text{ maximum BLAST score}}{100}$$

The product score takes into account both the degree of similarity between two sequences and the length of the sequence match. For example, with a product score of 40, the match will be exact within a 1% to 2% error, and, with a product score of 70, the match will be exact. Similar molecules are usually identified by selecting those which show product scores between 15 and 40, although lower scores may identify related molecules.

The results of northern analyses are reported a percentage distribution of libraries in which the transcript encoding HTRM occurred. Analysis involved the categorization of cDNA libraries by organ/tissue and disease. The organ/tissue categories included cardiovascular, dermatologic, developmental, endocrine, gastrointestinal, hematopoietic/immune, musculoskeletal, nervous, reproductive, and urologic. The disease categories included cancer, inflammation/trauma, fetal, neurological, and pooled. For each category, the number of libraries expressing the sequence of interest was counted and divided by the total number of libraries across all categories. Percentage values of tissue-specific and disease expression are reported in Table 3.

V. Extension of HTRM Encoding Polynucleotides

The full length nucleic acid sequence of SEQ ID NO:66-130 was produced by extension of an appropriate fragment of the full length molecule using oligonucleotide primers designed from this fragment. One primer was synthesized to initiate 5' extension of the known fragment, and the other primer, to initiate 3' extension of the known fragment. The initial primers were designed using OLIGO 4.06 software (National Biosciences), or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the target sequence at temperatures of about 68°C to about 72°C. Any stretch of nucleotides which would result in hairpin structures and primer-primer dimerizations was avoided.

Selected human cDNA libraries were used to extend the sequence. If more than one extension was necessary or desired, additional or nested sets of primers were designed.

High fidelity amplification was obtained by PCR using methods well known in the art. PCR was performed in 96-well plates using the PTC-200 thermal cycler (MJ Research, Inc.). The reaction mix contained DNA template, 200 nmol of each primer, reaction buffer containing Mg^{2+} , $(NH_4)_2SO_4$, and β -mercaptoethanol, Taq DNA polymerase (Amersham Pharmacia Biotech), ELONGASE enzyme (Life Technologies), and Pfu DNA polymerase (Stratagene), with the following parameters for primer pair PCI A and PCI B: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C. In the alternative, the parameters for primer pair T7 and SK+

were as follows: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 57°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C.

The concentration of DNA in each well was determined by dispensing 100 µl PICOGREEN quantitation reagent (0.25% (v/v) PICOGREEN; Molecular Probes, Eugene OR) dissolved in 1X TE and 0.5 µl of undiluted PCR product into each well of an opaque fluorimeter plate (Corning Costar, Acton MA), allowing the DNA to bind to the reagent. The plate was scanned in a Fluoroskan II (Labsystems Oy, Helsinki, Finland) to measure the fluorescence of the sample and to quantify the concentration of DNA. A 5 µl to 10 µl aliquot of the reaction mixture was analyzed by electrophoresis on a 1 % agarose mini-gel to determine which reactions were successful in extending the sequence.

The extended nucleotides were desalted and concentrated, transferred to 384-well plates, digested with CviJI cholera virus endonuclease (Molecular Biology Research, Madison WI), and sonicated or sheared prior to religation into pUC 18 vector (Amersham Pharmacia Biotech). For shotgun sequencing, the digested nucleotides were separated on low concentration (0.6 to 0.8%) agarose gels, fragments were excised, and agar digested with Agar ACE (Promega). Extended clones were religated using T4 ligase (New England Biolabs, Beverly MA) into pUC 18 vector (Amersham Pharmacia Biotech), treated with Pfu DNA polymerase (Stratagene) to fill-in restriction site overhangs, and transfected into competent *E. coli* cells. Transformed cells were selected on antibiotic-containing media, individual colonies were picked and cultured overnight at 37°C in 384-well plates in LB/2x carb liquid media.

The cells were lysed, and DNA was amplified by PCR using Taq DNA polymerase (Amersham Pharmacia Biotech) and Pfu DNA polymerase (Stratagene) with the following parameters: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 72°C, 2 min; Step 5: steps 2, 3, and 4 repeated 29 times; Step 6: 72°C, 5 min; Step 7: storage at 4°C. DNA was quantified by PICOGREEN reagent (Molecular Probes) as described above. Samples with low DNA recoveries were reamplified using the same conditions as described above. Samples were diluted with 20% dimethylsulphoxide (1:2, v/v), and sequenced using DYENAMIC energy transfer sequencing primers and the DYENAMIC DIRECT kit (Amersham Pharmacia Biotech) or the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (Perkin-Elmer).

In like manner, the nucleotide sequence of SEQ ID NO:66-130 is used to obtain 5' regulatory sequences using the procedure above, oligonucleotides designed for such extension, and an appropriate genomic library.

VI. Labeling and Use of Individual Hybridization Probes

Hybridization probes derived from SEQ ID NO:66-130 are employed to screen cDNAs, genomic DNAs, or mRNAs. Although the labeling of oligonucleotides, consisting of about 20

base pairs, is specifically described, essentially the same procedure is used with larger nucleotide fragments. Oligonucleotides are designed using state-of-the-art software such as OLIGO 4.06 software (National Biosciences) and labeled by combining 50 pmol of each oligomer, 250 μ Ci of [γ - 32 P] adenosine triphosphate (Amersham Pharmacia Biotech), and T4 polynucleotide kinase (DuPont NEN, Boston MA). The labeled oligonucleotides are substantially purified using a SEPHADEX G-25 superfine size exclusion dextran bead column (Amersham Pharmacia Biotech). An aliquot containing 10^7 counts per minute of the labeled probe is used in a typical membrane-based hybridization analysis of human genomic DNA digested with one of the following endonucleases: Ase I, Bgl II, Eco RI, Pst I, Xba I, or Pvu II (DuPont NEN).

10 The DNA from each digest is fractionated on a 0.7% agarose gel and transferred to nylon membranes (Nytran Plus, Schleicher & Schuell, Durham NH). Hybridization is carried out for 16 hours at 40°C. To remove nonspecific signals, blots are sequentially washed at room temperature under increasingly stringent conditions up to 0.1 x saline sodium citrate and 0.5% sodium dodecyl sulfate. After XOMAT-AR film (Eastman Kodak, Rochester NY) is exposed to the blots to film 15 for several hours, hybridization patterns are compared visually.

VII. Microarrays

A chemical coupling procedure and an ink jet device can be used to synthesize array elements on the surface of a substrate. (See, e.g., Baldeschweiler, supra.) An array analogous to a dot or slot blot may also be used to arrange and link elements to the surface of a substrate using 20 thermal, UV, chemical, or mechanical bonding procedures. A typical array may be produced by hand or using available methods and machines and contain any appropriate number of elements. After hybridization, nonhybridized probes are removed and a scanner used to determine the levels and patterns of fluorescence. The degree of complementarity and the relative abundance of each probe which hybridizes to an element on the microarray may be assessed through analysis of the 25 scanned images.

Full-length cDNAs, Expressed Sequence Tags (ESTs), or fragments thereof may comprise the elements of the microarray. Fragments suitable for hybridization can be selected using software well known in the art such as LASERGENE software (DNASTAR). Full-length cDNAs, ESTs, or fragments thereof corresponding to one of the nucleotide sequences of the 30 present invention, or selected at random from a cDNA library relevant to the present invention, are arranged on an appropriate substrate, e.g., a glass slide. The cDNA is fixed to the slide using, e.g., UV cross-linking followed by thermal and chemical treatments and subsequent drying. (See, e.g., Schena, M. et al. (1995) Science 270:467-470; Shalon, D. et al. (1996) Genome Res. 6:639-645.) Fluorescent probes are prepared and used for hybridization to the elements on the substrate. The 35 substrate is analyzed by procedures described above.

VIII. Complementary Polynucleotides

Sequences complementary to the HTRM-encoding sequences, or any parts thereof, are used to detect, decrease, or inhibit expression of naturally occurring HTRM. Although use of oligonucleotides comprising from about 15 to 30 base pairs is described, essentially the same
5 procedure is used with smaller or with larger sequence fragments. Appropriate oligonucleotides are designed using OLIGO 4.06 software (National Biosciences) and the coding sequence of HTRM. To inhibit transcription, a complementary oligonucleotide is designed from the most unique 5' sequence and used to prevent promoter binding to the coding sequence. To inhibit translation, a complementary oligonucleotide is designed to prevent ribosomal binding to the
10 HTRM-encoding transcript.

IX. Expression of HTRM

Expression and purification of HTRM is achieved using bacterial or virus-based expression systems. For expression of HTRM in bacteria, cDNA is subcloned into an appropriate vector containing an antibiotic resistance gene and an inducible promoter that directs high levels
15 of cDNA transcription. Examples of such promoters include, but are not limited to, the *trp-lac* (*tac*) hybrid promoter and the T5 or T7 bacteriophage promoter in conjunction with the *lac* operator regulatory element. Recombinant vectors are transformed into suitable bacterial hosts, e.g., BL21(DE3). Antibiotic resistant bacteria express HTRM upon induction with isopropyl beta-D-thiogalactopyranoside (IPTG). Expression of HTRM in eukaryotic cells is achieved by
20 infecting insect or mammalian cell lines with recombinant Autographica californica nuclear polyhedrosis virus (AcMNPV), commonly known as baculovirus. The nonessential polyhedrin gene of baculovirus is replaced with cDNA encoding HTRM by either homologous recombination or bacterial-mediated transposition involving transfer plasmid intermediates. Viral infectivity is maintained and the strong polyhedrin promoter drives high levels of cDNA transcription.
25 Recombinant baculovirus is used to infect Spodoptera frugiperda (Sf9) insect cells in most cases, or human hepatocytes, in some cases. Infection of the latter requires additional genetic modifications to baculovirus. (See Engelhard, E. K. et al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945.)

In most expression systems, HTRM is synthesized as a fusion protein with, e.g.,
30 glutathione S-transferase (GST) or a peptide epitope tag, such as FLAG or 6-His, permitting rapid, single-step, affinity-based purification of recombinant fusion protein from crude cell lysates. GST, a 26-kilodalton enzyme from Schistosoma japonicum, enables the purification of fusion proteins on immobilized glutathione under conditions that maintain protein activity and antigenicity (Amersham Pharmacia Biotech). Following purification, the GST moiety can be
35 proteolytically cleaved from HTRM at specifically engineered sites. FLAG, an 8-amino acid

peptide, enables immunoaffinity purification using commercially available monoclonal and polyclonal anti-FLAG antibodies (Eastman Kodak). 6-His, a stretch of six consecutive histidine residues, enables purification on metal-chelate resins (QIAGEN). Methods for protein expression and purification are discussed in Ausubel (1995, supra, ch 10 and 16). Purified HTRM obtained
5 by these methods can be used directly in the following activity assay.

X. Demonstration of HTRM Activity

HTRM activity is measured by its ability to stimulate transcription of a reporter gene, essentially as described in Liu, H.Y., et al (1997; EMBO J. 16:5289-5298.). The assay entails the use of a well characterized reporter gene construct, LexA_{op}-LacZ, that consists of LexA DNA
10 transcriptional control elements (LexA_{op}) fused to sequences encoding the *E. coli* β -galactosidase enzyme (LacZ). The methods for fusion gene construction, expression, and introduction into cells, and measurement of β -galactosidase enzyme activity, are well known to those skilled in the art. Sequences encoding HTRM are cloned into a plasmid that directs the synthesis of a fusion protein, LexA-HTRM, consisting of HTRM and a DNA binding domain derived from the LexA
15 transcription factor. The plasmid encoding the LexA-HTRM fusion protein is introduced into yeast cells along with the plasmid containing the LexA_{op}-LacZ reporter gene. The amount of β -galactosidase enzyme activity associated with LexA-HTRM transfected cells, relative to control cells, is proportional to the amount of transcription stimulated by the HTRM gene product.

20 XI. Functional Assays

HTRM function is assessed by expressing the sequences encoding HTRM at physiologically elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression vector containing a strong promoter that drives high levels of cDNA expression. Vectors of choice include pCMV SPORT (Life Technologies) and pCR3.1
25 (Invitrogen, Carlsbad CA), both of which contain the cytomegalovirus promoter. 5-10 μ g of recombinant vector are transiently transfected into a human cell line, preferably of endothelial or hematopoietic origin, using either liposome formulations or electroporation. 1-2 μ g of an additional plasmid containing sequences encoding a marker protein are co-transfected. Expression of a marker protein provides a means to distinguish transfected cells from nontransfected cells and
30 is a reliable predictor of cDNA expression from the recombinant vector. Marker proteins of choice include, e.g., Green Fluorescent Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser optics-based technique, is used to identify transfected cells expressing GFP or CD64-GFP, and to evaluate properties, for example, their apoptotic state. FCM detects and quantifies the uptake of fluorescent molecules that diagnose
35 events preceding or coincident with cell death. These events include changes in nuclear DNA

content as measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; down-regulation of DNA synthesis as measured by decrease in bromodeoxyuridine uptake; alterations in expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies; and alterations in plasma membrane composition as measured by the binding of fluorescein-conjugated Annexin V protein to the cell surface. Methods in flow cytometry are discussed in Ormerod, M. G. (1994) Flow Cytometry, Oxford, New York NY.

The influence of HTRM on gene expression can be assessed using highly purified populations of cells transfected with sequences encoding HTRM and either CD64 or CD64-GFP. CD64 and CD64-GFP are expressed on the surface of transfected cells and bind to conserved regions of human immunoglobulin G (IgG). Transfected cells are efficiently separated from nontransfected cells using magnetic beads coated with either human IgG or antibody against CD64 (DYNAL, Lake Success NY). mRNA can be purified from the cells using methods well known by those of skill in the art. Expression of mRNA encoding HTRM and other genes of interest can be analyzed by northern analysis or microarray techniques.

XII. Production of HTRM Specific Antibodies

HTRM substantially purified using polyacrylamide gel electrophoresis (PAGE; see, e.g., Harrington, M.G. (1990) *Methods Enzymol.* 182:488-495), or other purification techniques, is used to immunize rabbits and to produce antibodies using standard protocols.

Alternatively, the HTRM amino acid sequence is analyzed using LASERGENE software (DNASTAR) to determine regions of high immunogenicity, and a corresponding oligopeptide is synthesized and used to raise antibodies by means known to those of skill in the art. Methods for selection of appropriate epitopes, such as those near the C-terminus or in hydrophilic regions are well described in the art. (See, e.g., Ausubel, 1995, supra, ch. 11.)

Typically, oligopeptides 15 residues in length are synthesized using an ABI 431A Peptide Synthesizer (Perkin-Elmer) using fmoc-chemistry and coupled to KLH (Sigma-Aldrich, St. Louis MO) by reaction with N-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS) to increase immunogenicity. (See, e.g., Ausubel, 1995, supra.) Rabbits are immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. Resulting antisera are tested for anti-peptide activity by, for example, binding the peptide to plastic, blocking with 1% BSA, reacting with rabbit antisera, washing, and reacting with radio-iodinated goat anti-rabbit IgG.

XIII. Purification of Naturally Occurring HTRM Using Specific Antibodies

Naturally occurring or recombinant HTRM is substantially purified by immunoaffinity chromatography using antibodies specific for HTRM. An immunoaffinity column is constructed by covalently coupling anti-HTRM antibody to an activated chromatographic resin, such as

CNBr-activated SEPHAROSE (Amersham Pharmacia Biotech). After the coupling, the resin is blocked and washed according to the manufacturer's instructions.

Media containing HTRM are passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of HTRM (e.g., high ionic strength buffers in the presence of detergent). The column is eluted under conditions that disrupt antibody/HTRM binding (e.g., a buffer of pH 2 to pH 3, or a high concentration of a chaotrope, such as urea or thiocyanate ion), and HTRM is collected.

XIV. Identification of Molecules Which Interact with HTRM

HTRM, or biologically active fragments thereof, are labeled with ^{125}I Bolton-Hunter reagent. (See, e.g., Bolton et al. (1973) *Biochem. J.* 133:529.) Candidate molecules previously arrayed in the wells of a multi-well plate are incubated with the labeled HTRM, washed, and any wells with labeled HTRM complex are assayed. Data obtained using different concentrations of HTRM are used to calculate values for the number, affinity, and association of HTRM with the candidate molecules.

Various modifications and variations of the described methods and systems of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with specific preferred embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in molecular biology or related fields are intended to be within the scope of the following claims.

Table 1

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
1	66	001106	U937NOT01	001106 (U937NOT01), 1291142 (BRAINOT11), 2590425 (LUNGNOT22), 1300570 (BRSTNOT07)
2	67	004586	HMC1NOT01	004586 (HMC1NOT01), 3889843 (BRSTTUT16), 1432988 (BEPINON01), 788995 (PROSTUT03), 1605475 (LUNGNOT15)
3	68	052927	FIBRNOT01	052927 (FIBRNOT01), 2518848 (BRAITUT21), 3520218 (LUNGNOT03), 086878 (LIVRNOT01)
4	69	082843	HUVESTB01	082843 (HUVESTB01), 4008105 (ENDCNOT04), 2083528 (UTRSNOT08), 2345764 (TESTTUT02), 3771780 (BRSTNOT25), 190782 (CONUTUT01), 2206259 (SPLNFET02), 2509193 (CONUTUT01)
5	70	322349	EOSIHET02	322349 (EOSIHET02), 3686018 (HEAANOT01), 1853592 (LUNGFET03), 815966 (OVARUT01), 1505002 (BRAITUT07), 1511883 (LUNGNOT14), 2232826 (PROSNOT16)
6	71	397663	PITUNOT02	397663 (PITUNOT02), 491141 (HMT2AGT01), 3809879 (CONITUT01), 3562349 (SKINNOT05), 1518413 (BLADTUT04), 3600151 (DRGTNOT01), 2474103 (THPINOT03), 2105304 (BRAITUT03), 2187330 (PROSNOT26), 1781572 (PGANNON02), 2056258 (BEPINOT01), 1888065 (BLADTUT07)
7	72	673766	CRBLNOT01	673766 (CRBLNOT01), 2494421 (ADRETUT05), 3267748 (BRAINOT20), 2194042 (THYRTUT03), 3186455 (THYMNON04), 1712236 (PROSNOT16), 1844092 (COLANOT08), 1602283 (BLADNOT03), 033357 (THPINOB01), 1995828 (BRSTTUT03), 1485594 (CORPNOT02)
8	73	1504753	BRAITUT07	1504753 (BRAITUT07), 633939 (NEUTGMT01), 2741379 (BRSTTUT14), 2959661 (ADRENOT09), 3483904 (KIDNNOT31), 999401 (KIDNUT01), 1965504 (BRSTNOT04), 588535 (UTRSNOT01)
9	74	1760185	PITUNOT03	1760085 (PITUNOT03), 1914471 (PROSTUT04), 836831 (PROSNOT07), 729798 (LUNGNOT03), 1290847 (BRAINOT11), 1492387 (PROSNOT01), 1368472 (SCORNON02)

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
10	75	1805061	SINTNOT13	1805061 (SINTNOT13), 1435949 (PANCNOT08), 086122(LIVRNOT01) 1482366 (CORPNOT02), 1835310 (BRAINON01), 1333758 (COLANNOT13), 3521449 (LUNGNON03)
11	76	1850120	LUNGFET03	1850120 (LUNGFET03), 3126350 (LJUNGUT12), 786916 (PROSNOT05) 2899740 (DRGCNOT01), 1259221 (MENITUT03), 1334740 (COLANNOT13), 2466350 (THYRNOT08)
12	77	1852290	LUNGFET03	1852290 (LUNGFET03), 2901081 (DRGCNOT01), 1384842 (BRAITUT08) 1293541 (PGANNOT03), 1964126 (BRSTNOT04)
13	78	1944530	PITUNOT01	1944530 (PITUNOT01), 2808142 and 2809196 (BLADTUT08), 2961779 (ADRENOT09)
14	79	2019742	CONNNOT01	2019742 (CONNNOT01), 2968014 (SCORNOT04), 168472 (LIVRNOT01) 1875993 (LEUKNOT02), 1522480 (BLADTUT04), 1418496 (KIDNNOT09), 149730 (FIBRNGT02)
15	80	2056042	BEPINOT01	2056042 (BEPINOT01), 3097391 (CERVNOT03), 1985203 (LUNGAST01) 1962619 (BRSTNOT04), 1335716 (COLNNOT13)
16	81	2398682	THPIAZT01	2398682 (THPIAZT01), 159706 (ADENINB01), 2443910 (THP1NOT03) 2382189 (ISLTNOT01), 2288661 (BRAINON01), 1864422 (PROSNOT19)
17	82	2518753	BRAITUT21	2518753 (BRAITUT21), 4001219 (INT2AZS07), 2606361 (LUNGUT07) 449043 (TLYMNOT02), SAEA01390
18	83	2709055	PONSASZT01	2709055 (PONSASZT01), 2309703 (NGANNOT01), 1661042 (URETTUT01), 2761284 (ESOGTUT02), 2469634 (THPINOT03), SBLA03183, SBLA00549 SBLA00975
19	84	2724537	LJUNGUT10	2724537 (LJUNGUT10), 3869823 (BMARNOT03), 952779 (SCORNON01), 2049127 (LIVRFET02), 1824284 (GBLATUT01), 1870588 and 1869666 (SKINBIT01), 2626505 (PROSTUT12), SAEA03404, SAEA01744 SAEA01672, SAEA10045, SAPA04072, SAPA00149

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragment
20	85	025818	SPLNFET01	025818H1, 025818X12, and 025818X3 (SPLNFET01), 783259H1 (MYOMNOT01), 826162R1 (PROSNOT06)
21	86	438283	THYRNOT01	438283H1 and 438283X29 (THYRNOT01), SAGA01136F1, SAGA01671F1, SAGA02704F1, SAGA03722F1, SZZZ01038R1
22	87	619699	PGANNOT01	619699H1, 619699X11, and 619699X18 (PGANNOT01), 646198T6 (BRSTTUT02), 1322305X20F1 (BLADNOT04), 1724376F6 (PROSNOT14)
23	88	693452	SYNORAT03	118140R1 (MUSCNOT01), 693452H1 and 693452R6 (SYNORAT03), 2455538F6 and 2455538H1 (ENDANOT01), 4500333H1 (BRAVTXT02)
24	89	839651	PROSTUT05	729341X12 (LUNGNOT03), 839651CT1, 839651H1, and 839651X55 (PROSTUT05), 839651X60 (PROSTUT05)
25	90	1253545	LUNGFET03	1253545H1 and 1254914F6 (LUNGFET03), 1806337X13F1 and 1807402X11F1 (SINTNOT13), 2179882X22F1 (SININOT01), 2592938F6 (LUNGNOT22), 2840018F6 (DRGLNOT01)
26	91	1425691	BEPINON01	2727135H1 (OVARTUT05), 587126X29R1, 588598X17, and 587126F1 (UTRSNOT01), 1714529F6 (UCMCNOT02), 1381341F6 (BRAITUT08), 1273513F6 (TESTTUT02), 060265R1 (LUNGNOT01), 1459659F1 (COLNFET02), 043139R1 (TBLYNOT01), 1425691H1 (BEPINON01)

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
27	92	1484257	CORPNOT02	400685H1, 404702F1, 404702R6, 404702X45C1, 404702X47C1, and 404702X48C1 (TMLR3DT01), 1484257H1 (CORPNOT02), 3396312H1 (UTRSNOT16)
28	93	1732368	BRSTTUT08	920006H1 (RATRNOT02), 1732368F6 and 1732368H1 (BRSTTUT08), 2607269T6 (LUNGUT07), 2654363F6 (THYMNOT04)
29	94	1870914	SKINBIT01	1549551R6 (PROSNOT06), 1575349H1 (LNODNOT03), 1870914H1 (SKINBIT01), 2365851T6 (ADRENOT07), SBKA00149F1
30	95	1910984	CONNTUT01	859876X12 (BRAITUT03), 1234976H1 and 1241845H1 (LUNGNOT03), 1910984F6 and 1910984H1 (CONNTUT01), 3276505H1 (PROSBPT06)
31	96	1943040	HIPONOT01	824144R1 (PROSNOT06), 930281H1 (CERVNOT01), 1420545H1 (KIDNNOT09), 1784405H1 (BRAINOT10), 1943040H1 and 1943040R6 (HIPONOT01), 2122271H1 (BRSTNOT07), 2729723H1 (OVRTUT04)
32	97	2076520	ISLTNOT01	419755R1 (BRSTNOT01), 954937R1 (KIDMNOT05), 1460268H1 (COINFET02), 1599016H1 (BLADNOT03), 2076520H1 (ISLTNOT01), 2082255F6 (UTRSNOT08), 2184150F6 (SININOT01), 2884394F6 (SINJNOT02), 3726575H1 (BRSTNOT23), 3752466H1 (UTRSNOT18), 3764971H1 (BRSTNOT24), 4412005H1 (MONOTXT01)

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
33	98	2291241	BRAINON01	2291241CT1 and 2291241H1 (BRAINON01), 2500586H1 (ADRETUT05)
34	99	2329692	COLNNOT11	158014F1 (ADENINB01), 1519462F1 (BLADTUT04), 1543875R1 (PROSTUT04), 2329692H1, 2331530R6, and 2331530T6 (COLNNOT11), 2478291F6 (SMCANOT01)
35	100	2474110	THP1NOT03	863265H1 (BRAITUT03), 1313444F1 (BLADTUT02), 1872631T6 and 1872869F6 (LEUKNOT02), 2061219R6 (OVARNOT03), 2171863H1 (ENDCNOT03), 2474110H1 (THP1NOT03), 2690250H1 (LUNGNOT23), 2812791F6 (OVARNOT10)
36	101	2495790	ADRETUT05	1360349T1 (LUNGNOT12), 1689792H1 (PROSTUT10), 1795321H1 (PROSTUT05), 1905521F6 (OVARNOT07), 1907168F6 (OVARNOT07), 2495790H1 (ADRETUT05), 2587542F6 (BRAITUT22)
37	102	2661254	ADRENOT08	1241850H1 (LUNGNOT03), 1545867R1 (PROSTUT04), 2325561H1 (OVARNOT02), 2661254H1 (ADRENOT08), 2751457H1 (THP1AZS08)
38	103	2674047	KIDNNOT19	489330H1 (HNT2AGT01), 2059316R6 (OVARNOT03), 2059316T6 (OVARNOT03), 2674047F6 and 2674047H1 (KIDNNOT19), 2805474H1 (BLADTUT08), 3076605H1 (BONEUNT01), 3080137T6 (BRAIUNT01)

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
39	104	2762174	BRAINOS12	2573448T3 (HIPOAZT01), 2762174H1 (BRAINOS12), SBNA00508F1, SBNA01683F1, SBNA00674F1, SBNA00857F1
40	105	2765991	BRSTNOT12	082008R6 (HUVESTB01), 2127491T6 (KIDNNOT05), 2765991F6 and 2765991H1 (BRSTNOT12), 3147681H1 (PENCNOT05), SHAH01537F1, SHAH01356F1
41	106	2775157	PANCNOT15	2325410H1 (OVARNOT02), 2506671F6 and 2506671T6 (CONUTUT01), 2775157F6 and 2775157H1 (PANCNOT15), 3376091F6 (PENGNOT01), 3412063H1 (BRSTTUS08)
42	107	2918375	THYMFET03	227782F1 (PANCNOT01), 1225559H1 (COLNTUT02), 1511458T1 (LUNGNOT14), 2918375H1 (THYMFET03)
43	108	3149729	ADRENON04	605315F1 (BRSTTUT01), 3149729CT1 and 3149729H1 (ADRENON04)
44	109	3705895	PENCNOT07	744201R1 (BRAITUT01), 2550322H1 (LUNGUT06), 3705895H1 (PENCNOT07)

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
45	110	003256	HMC1NOT01	003256H1, 003256R6, 003256T6, 003256X305F1, 003256X313F, 003256X315F1, and 009404H1 (HMC1NOT01), 43104R1 (TBLYNOT01), 413017F1 (BRSTNOT01)
46	111	156986	THP1PLB02	010084F1 and 012909H1 (THP1PLB01), 156986H1 and 156986R1 (THP1PLB02), 1320255F1 (BLADNOT04), 1512255F1 (LUNGNOT14), 2061923T6 (OVARNOT03), 2398787F6 (THP1AZT01), 2517160H2 (LIVRTUT04)
47	112	319415	EOSIHET02	285773H1, 285773R1, 319415H1, and 319415X19F1 (EOSIHET02), 1231455H1 (BRAITUT01), 1804042F6 (SINTNOT13), 1878858F6 (LEUKNOT03)
48	113	635581	NEUTGMT01	635581H1 (NEUTGMT01), 3045776F6 (HEANOT01)
49	114	921803	RATRN02	921803H1 (RATRN02), 1275128T6 (TESTTUT02), 1709959F6 (PROSNOT16), 2416547F6 (HNT3AZT01), 3016146H1 (MUSCNOT07), 3577260H1 (BRONNOT01)
50	115	1250492	LUNGFET03	691921X14F1 (LUNGTUT02), 1250492F6, 1250492H1, and 1252265F2 (LUNGFET03), 1361644F6 (LUNGNOT12), 3049358F6 (LUNGNOT25), 4044523H1 and 4048275H1 (LUNGNOT35), 4145295H1 (SINITUT04)
51	116	1427838	SINTBST01	1261181H1 (SYNORAT05), 1427838H1 and 1427838T1 (SINTBST01), 1733769T6 (BRSTTUT08), 2551854H1 (LUNGTUT06)
52	117	1448258	PLACNOT02	1448258H1 and 1448258R1 (PLACNOT02), 1484126F1 (CORPNOT02), 1856631F6 and 1856631X11F1 (PROSNOT18), 2690070F6 (LUNGNOT23), SAMA00131F1 and SAMA00146F1

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
53	118	1645941	PROSTUT09	831680R6 (PROSTUT04), 1645941F6 and 1645941H1 (PROSTUT09), 1748682F6 (STOMTUT02), 1870831F6 (SKINBIT01), 1877907F6 (LEUKNOT03), 2310427R6 (NGANNOT01)
54	119	1646005	PROSTUT09	1646005H1, 1646005X309F1, 1646005X312F1 and 1646883F6 (PROSTUT09), SZA02276F1
55	120	1686561	PROSNOT15	1234124H1 (LUNGFET03), 1299156F6 (BRSTNOT07), 1425185R1 (BEPINON01), 1544751T1 (PROSTUT04), 1686561H1 (PROSNOT15), 2723108H1 (LUNGTUT10), 2752156H1 (THPLAZS08), 3335850F6 (BRAIFET01), 3502259H1 (ADRENOT11), 3857461H1 (LNODNOT03), 5069547H1 (PANCNOT23)
56	121	1821233	GBLATUT01	030744H1 (THPINOB01), 1272043F1 (TESTTUT02), 1419549F1 (KIDNNOT09), 1433773R1 (BEPINON01), 1482848F1 (CORPNOT02), 1821233H1 (GBLATUT01), 1869022H1 (SKINBIT01)
57	122	1877278	LEUKNOT03	1871148F6 (SKINBIT01), 1877278H1 (LEUKNOT03), 2097362T6 (BRAITUT02), 3124246T6 (LNODNOT05), 3450007R6 (UTRSNON03), 4894340H1 (LIVRTUT12), SAE02108R1
58	123	1880692	LEUKNOT03	1880692H1 (LEUKNOT03), SBA00446F1, SARA03727F1

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
59	124	2280456	PROSNON01	1557906F6 (BLADTUT04), 2280456H1 (PROSNON01), 2799446F6 (NPOLNOT01), 3519009H1 (LUNGNON03)
60	125	2284580	BRAINON01	783560H1 (MYOMNOT01), 1215190T2 (BRSTTUT01), 1458188F1 (COLNFET02), 2284580H1 (BRAINON01), 2398366F6 (THP1AZT01), 2469268H1 (THPINOT03)
61	126	2779172	OVARTUT03	487548H1 and 487548R6 (HNT2AGT01), 1421684F1 (KIDNNOT09), 2172754F6 (ENDCNOT03), 2672062F6 (ESOGTUT02), 2779172F6 and 2779172H1 (OVARTUT03), 2935502F6 (THYMFET02), 3206879F6 (PENCNOT03)
62	127	3279329	STOMFET02	885282R6 and 885282T1 (PANCNOT05), 901139R1 (BRSTTUT03), 1655530F6 (PROSTUT08), 1818669T6 (PROSNOT20), 2380664F6 (ISLTNOT01), 2921229H1 (SININOT04), 3279329H1 (STOMFET02), 3451425R6 (UTRSNON03)
63	128	3340290	SPLNNOT10	102935H1 (ADRENOR01), 1363193F6 (LUNGNOT12), 1674514H1 (BLADNOT05), 2271374H1 (PROSNON01), 2827770H1 (TLYMNOT03), 3340290H1 (SPLNNOT10), 4556330H1 (KERAUNT01)
64	129	3376404	PENGNOT01	3376404H1, 3376404X300U1, 3376404X310U1, and 3376404X323U1 (PENGNOT01), 3741323X302B1 (MENTNOT01)
65	130	4173111	SINTNOT21	1337315F6 (COLNNOT13), 2486184F6 (CONUTUT01), 4173111H1 (SINTNOT21), 4750042H1 (SMCRUNT01)

Table 2

Protein SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
1	155	S9, S16, T25, S37, S56, S57, S81, S114, T152		G38-I73	sigma-54 interaction protein	BLOCKS
2	152	S6, T83, S103, T121, S136		H99-R112	LUPUS La protein	PRINTS
3	304	S30, S61, S94, T109, S132, S133, T183, T236, S277, S289	N65, N294	C228-C368 C231-I255	zinc finger/RING finger protein	PFAM, BLOCKS
4	178	T8, S48, S102, Y121, T144		N18-P32	histone H3 protein	PRINTS
5	301	T58, T70, T85, S148, T165, S256, T272, S281	N191	K21-F38	filaggrin structural protein	PRINTS
6	250	S99, S126, S142, S155, T182		F203-V214	maspin/breast tumor suppressor protein	PRINTS
7	371	T25, S46, S96, T123, S128, T144, S163, S167, S205, S221, T350	N203, N222, N307, N348	EQ165-Y185 K152-L192	human/leucine zipper/CRE protein	BLAST, BLOCKS, PRINTS

Table 2 cont.

Protein SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
8	148	T35, S41, S92, S105	N144		TSC-22 transcription factor	BLAST
9	127	T69	N53	M1-E16	Ribosomal protein S6	PFAM
10	383	S22, T34, S53, S140, T155, T183, S225, T263, S273, S300, S308, T369, S375	N127	Q7-K112	PH-domain protein	Pfam
11	254	T57, S62, S92, S143, S148, T166, T176, S180, T187, S191, S194, T221			cyclin-dependent-k inase binding protein	BLAST
12	305	S65, T88, S146, S230, S248, S272	N221	G84-N271	ribosomal protein L2	PFAM, BLOCKS
13	230	T34, T49, S54, S122, T123, T150, S182, T209	N86, N130, N199	C155-C191	zinc finger/RING finger protein	PFAM, BLOCKS, MOTIFS
14	292	S2, T61, T89, T193, S223, S224, S225, S238, S288	N47, N101, N166, N259	A124-I145	FOS transforming protein	PRINTS

Table 2 cont.

Protein SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
15	232	T58, S72, S127, S149, T154, S191, S199, T203, T204	N56, N183, N187	E39-F73	tropomyosin	BLOCKS PRINTS
16	376	T5, T34, S53, T70, S81, T86, S105, S256, T287, T288, T310, S331, S364, S369, T365		Q97-C135	RecA DNA repair protein	BLOCKS BLAST
17	204	T100, T118, T157, S187, S199		L179-H200	annexin	PRINTS
18	713	S46, T64, T71, T95, S96, T129, T171, S260, S286, T345, S438, S485, T527, T541, Y567, Y593, S644, T656	N110, N453, N460, N595	L563-L576 L583-I596	RSP-1 /Ras-signaling protein	BLAST, PRINTS
19	360	S22, T51, S69, T106, S133, S206, T232, S248			Nucleolar protein Surf-6	BLAST
20	196	S38 S69 T23 T30 S73 S183 S37 T84	N9 N51	E76-L91 R35-K58	Helix-loop-helix protein HES-1	MOTIFS BLOCKS BLAST

Table 2 cont.

Protein Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
21	540	T136 S34 S69 S189 T322 S411 T7 S66 S75 T139 S193 S197 S205 T285 S324 S328 S380 S425	N240 N443	C230-H252, C260- H280, C288-H309, C316-H336, C344- H364, C372-H392, C400-H420, C428- H448, C456-H476, C484-H504, C512- H532	zinc finger protein	MOTIFS BLAST PRINTS
22	549	S123 S22 S182 T319 T465 S161 T205 S208 S332 S392 S459 S534	N167 N335 N422	C214-H234, C242- H262, C270-H290, C298-H318, C326- H346, C354-H374, C382-H402, C410- H430, C438-H458, C466-H486, C494- H514, C522-H542	zinc finger protein ZNF43	MOTIFS BLAST PRINTS
23	361	S244 T254 S8 S58 S180 S193 T269 T283 S284 T26 S45 S174 T254 S314		C139-L163 C227-K263	DNA binding protein	BLOCKS BLAST
24	241	S82 S62 S119 T147 Y111		C52-H75, C83- H105, C113-H133, C141-H161, C172- H193	zinc finger protein PZF	MOTIFS PRINTS BLAST

Table 2 cont.

Protein Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
25	576	S90 T371 S56 T183 T195 S203 S316 T318 S347 S354 S432 S548 S37 S82 S281 T325 S343 S409 S414 S447 S466 T481 S502 S570 Y323	N42 N312 N339 N498	C507-I543, L168- L189, E262-R278	transcription factor	MOTIFS PRINTS BLOCKS BLAST
26	408	S74 S197 T226 S247 T289 S328 S338 S353 S386 S394 T14 S199 S234 T388	N245 N253	G164-R175	transcription factor	PRINTS BLAST
27	810	S392 S113 S155 S185 S225 S262 S283 T298 S342 S433 T449 T665 T695 S728 T756 T801 T79 T190 S377 T438 Y397		C315-H335, C343- H363, C371-H391, C399-H419, C427- H447, C455-H475, C483-H503, C511- H531, C539-H559, C567-H587, C595- H615, C623-H644, C726-H747	zinc finger protein Miz-1	MOTIFS PRINTS BLOCKS
28	324	S72 T189 S209 T223 S279 S302 S156 T182 S316 Y277	N187	C74-R85	Hormone-binding transcription factor protein	PRINTS BLAST
29	292	S242 T41 S136 S137 T176 T200 S205 S284 T52 S61	N229	G62-S69	putative nucleotide-binding protein	MOTIFS PRINTS BLAST

Table 2 cont.

Protein Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
30	259	T79 S99 S180 T20 S152 S241		C71-H92, C43-C71	zinc finger protein	MOTIFS BLOCKS BLAST
31	97	S52		C15-L43	DNA-binding protein	MOTIFS BLOCKS BLAST
32	812	T239 T16 S55 T56 T104 S126 S127 T156 S176 T249 S268 T269 S330 T394 S450 T484 S583 S652 S658 S795 S33 S235 T314 S343 T730 S804	N45 N93 N165 N805	E418-S450	cell cycle protein	BLOCKS BLAST
33	392	T22 S30 T43 S55 S108 T140 S156 S318 T320 S343 S120 S270 S311	N277		TRAF family member-associated NF-kB activator TANK	BLAST
34	60	T49 T30 S50		I2-S55	DNA-binding protein	BLOCKS BLAST
35	209	S21 S57 T93	N67	F160-N179 S151-G185	cellular nucleic acid binding protein	PRINTS BLOCKS BLAST
36	257	T178 S187 S230 T249	N65	Y33-F44 S187-L205	cell-cycle control protein Hst2p	PRINTS BLOCKS BLAST

Table 2 cont.

Protein Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
37	138	T106 T3 S27 S46		E108-Q124	nucleic acid- binding protein	BLOCKS BLAST
38	999	T54 S634 S89 S126 S335 S414 S442 S451 T512 T762 T792 T858 S890 T97 T994 T205 S233 T274 T491 S525 S534 T577 T600 S610 S615 S634 S677 T951 S961 Y152 Y458 Y686 Y815	N43 N532 N672 N749 N818 N943	L574-L595 L647-L668	DNA-binding protein	MOTIFS BLAST
39	377	T142 T254 T48 T138 S292 S71 S74 S108 S114 T138 S222 S250 T332 T364		C130-H150, C158- H178, C186-H206, C214-H234, C242- H262, C270-H290, C296-H316, C324- H344, C352-H372	zinc finger protein ZNF132	MOTIFS PRINTS BLOCKS BLAST
40	324	S28 S214 S16 S81 S114 T225 T33 S44 T66 S203 S209 T229	N47	R26-S37 S77-L115	transcription regulatory protein IRLB	PRINTS BLOCKS BLAST
41	270	S16 T123 T141 T199 S9 S52 S90 T128 T175 S194 S214	N22 N109 N192	V218-L242 P250-Q263		MOTIFS BLOCKS PRINTS

Table 2 cont.

Protein Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
42	252	T20 S48 S89 S101 T127 S218 T121 S126 T152	N33 N46 N216 N230	Y9-L18, S68-F88, D159-S168	cell-cycle control protein	PRINTS BLAST
43	228	T50 T107 T2 S42 S201 T31 S51 T52 T103 T107 T134 T143 T206 S210 T215	N132 N141 N165 N197	A38-S51, Q65- P100, S59-K89	Transcriptional Repressor Protein	PRINTS BLOCKS BLAST
44	117	T93 T11		A86-E104	CCAAT-Binding Transcription factor	PRINTS BLAST
45	252	S83 T2 S57 T159 S250 Y102	N197	M1-S29 A85-K123	Ribosomal protein	BLOCKS MOTIFS
46	530	T177 S234 S461 S519 T24 T238	N217 N227	TM Domains: Y147-A167 Y242-L262 L306-F325 L332-L351 S379-F399 L470-F489	melibiose carrier protein	BLAST MOTIFS HMM

Table 2 cont.

SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
47	355	S7 S21 T127 S213 T279 S134 T276 S315 S331 S334 Y193 Y300	N37 N192 N263 N268 N337	I42-E69 W160-E187 G171-G200 N234-I256	Myelin P0 Protein	BLOCKS, PRINTS MOTIFS, IMM
48	136	T109 S130 T5 T69 T40 S121			geminin	BLAST, MOTIFS
49	235	T138 T142 S180 S230 S111 S120 S137 T224	N140 N198	ATP/GTP binding: G9-T16	PTB-associated splicing factor	BLAST MOTIFS
50	70	T2 S64			ninjurin	BLAST MOTIFS
51	169	T128 T26 S96			B locus M Beta chain 1	BLAST, MOTIFS
52	359	S55 S78 T161 S245 T292 T350 T57 T130 T289	N105	E205-S242 E271-V294	ribosomal protein S6 kinase 2	BLAST, MOTIFS BLOCKS, PRINTS, PFAM
53	545	S235 T317 S47 S73 S114 S146 S184 S236 S241 S394 S538 S2 T84 S109 S124 T230 S231 S266 S340 T360 S379 S525	N45 N139 N431 N478 N511	K88-I106 A333-K362	ribosomal protein	MOTIFS BLOCKS PRINTS

Table 2 cont.

SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
54	99	T90 T43 T76			ORF E4	BLAST, MOTIFS
55	565	S27 S56 S132 T152 T197 S319 T411 T429 S475 T66 S156 S303 T390 S463 Y549	N2 N55 N165		Sec1 precursor	BLAST, MOTIFS
56	197	S65 T23 S102 S19 T60 T61 S136 S147	N20		Regulatory protein	BLAST, MOTIFS
57	321	S91 S119 T139 S283 S147 T300 Y238	N103 N194		putative ras effector Norel	BLAST, MOTIFS
58	356	T45 S85 S93 S95 T103 S114 T142 S168 T317 S340 S49 S58 T236 S258 S314 Y12 Y296	N91 N312		weak similarity to S. cerevisiae intracellular transport protein	BLAST MOTIFS
59	299	S273 T81 S116 S120 T122 S146 S86 S151 T210 S225 T268			PI3 Kinase P85 Regulator	MOTIFS, PRINTS
60	293	T34 S218 S247 S290 S291 T240 S79 S145 T156 T199 S204 S283	N152	V47-V71 K86-F93	RNA-binding protein	BLAST, MOTIFS, BLOCKS, PFAM

Table 2 cont.

Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
61	777	S81 S128 S141 T230 S315 S342 S352 T519 S564 S576 S684 T699 T758 T205 S213 S236 S294 S397 T417 S470 S515 T560 S640 T746	N228 N281 N319 N453 N481 N636 N682		Zinc finger helicase	BLAST, MOTIFS
62	97	T83		C20-C28	ferredoxin	MOTIFS
63	308	S15 S81 T97 T102 S103 S135 S200 S238 S28 S131 T154 S171 S186 Y232	N58 N78 N95 N198 N236		ubiquitin- conjugating enzyme	BLAST, MOTIFS
64	290	S121 S165 S167 S248 S17 T188 T207 Y86 Y203	N55 N79	M1-A22 C60-C76 C225-C235 W249-I272	prostasin	BLAST, MOTIFS, BLO CKS, PRINTS PFAM, HMM
65	198	S7 S9 S56 T115 T34 T86	N183		transcriptional regulator	BLAST MOTIFS

TABLE 3

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
66	Nervous (0.256) Reproductive (0.209)	Cancer (0.442), Inflammation (0.279), Proliferative/Fetal (12%)	pBlueScript
67	Reproductive (0.274) Cardiovascular (0.194)	Cancer (0.484), Inflammation (0.145), Proliferative/Fetal (0.194)	pBlueScript
68	Reproductive (0.231) Cardiovascular (0.205)	Cancer (0.385), Inflammation (0.231), Proliferative/Fetal (0.205)	pBlueScript
69	Reproductive (0.215) Hematopoietic/Immune (0.190)	Cancer (0.397), Inflammation (0.314), Proliferative/Fetal (0.215)	pBlueScript
70	Reproductive (0.367) Cardiovascular (0.122)	Cancer (0.489), Inflammation (0.233), Proliferative/Fetal (0.189)	pBlueScript
71	Reproductive (0.292) Nervous (0.142)	Cancer (0.469), Inflammation (0.257), Proliferative/Fetal (0.177)	pSPORT1
72	Reproductive (0.261) Nervous (0.157)	Cancer (0.493), Inflammation (0.194), Trauma (0.142)	pSPORT1
73	Reproductive (0.343) Hematopoietic/Immune (0.200)	Cancer (0.457), Inflammation (0.257), Trauma (0.229)	pINCY
74	Reproductive (0.320) Nervous (0.160)	Cancer (0.507), Inflammation (0.187), Proliferative/Fetal (0.133)	pSPORT1
75	Gastrointestinal (0.300) Nervous (0.250)	Cancer (0.400), Inflammation (0.300)	pINCY
76	Reproductive (0.262) Nervous (0.180)	Cancer (0.443), Inflammation (0.262), Proliferative/Fetal (0.230)	pINCY
77	Reproductive (0.283) Nervous (0.151)	Cancer (0.509), Inflammation (0.208), Trauma (0.132)	pINCY

TABLE 3 cont.

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
78	Cardiovascular (0.300) Nervous (0.200)	Cancer (0.450), Inflammation (0.200)	pBlueScript
79	Reproductive (0.270) Cardiovascular (0.150)	Cancer (0.440), Inflammation (0.180), Proliferative/Fetal (0.150)	pINCY
80	Reproductive (0.271) Cardiovascular (0.153)	Cancer (0.506), Inflammation (0.176), Proliferative/Fetal (0.188)	pSPORT1
81	Hematopoietic/Immune (0.312) Reproductive (0.219)	Cancer (0.344), Inflammation (0.344), Proliferative/Fetal (0.281)	pINCY
82	Nervous (0.250) Hematopoietic/Immune (0.188)	Cancer (0.500), Inflammation (0.438), Proliferative/Fetal (0.188)	pINCY
83	Hematopoietic/Immune (0.276) Reproductive (0.276)	Cancer (0.552), Inflammation (0.310)	pINCY
84	Reproductive (0.309) Nervous (0.144)	Cancer (0.526), Inflammation (0.247), Proliferative/Fetal (0.134)	pINCY
85	Reproductive (0.315) Nervous (0.152) Cardiovascular (0.130)	Cancer (0.522) Fetal (0.174) Inflammation (0.141)	pBLUESCRIPT
86	Reproductive (0.545) Hematopoietic/Immune (0.182) Gastrointestinal (0.182)	Cancer (0.636) Fetal (0.273) Inflammation (0.182)	pBLUESCRIPT
87	Reproductive (0.218) Nervous (0.200) Hematopoietic/Immune (0.200)	Cancer (0.509) Inflammation (0.236) Fetal (0.164)	pSPORT1
88	Nervous (0.296) Reproductive (0.185) Hematopoietic/Immune (0.148)	Cancer (0.407) Fetal (0.259) Inflammation (0.222)	pSPORT1

TABLE 3 cont.

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
89	Reproductive (0.339) Nervous (0.161) Gastrointestinal (0.145) Cardiovascular (0.145)	Cancer (0.613) Fetal (0.145) Inflammation (0.129)	pSPORT1
90	Cardiovascular (0.278) Gastrointestinal (0.204) Reproductive (0.185)	Cancer (0.519) Inflammation (0.204) Fetal (0.148)	pINCY
91	Reproductive (0.228) Nervous (0.149) Gastrointestinal (0.146)	Cancer (0.411) Inflammation (0.343) Fetal (0.240)	pT7T3
92	Reproductive (0.240) Hematopoietic/Immune (0.160) Gastrointestinal (0.160)	Cancer (0.460) Inflammation (0.260) Fetal (0.180)	pINCY
93	Reproductive (0.333) Cardiovascular (0.200) Hematopoietic/Immune (0.133)	Inflammation (0.533) Cancer (0.400) Fetal (0.133)	pINCY
94	Reproductive (0.230) Gastrointestinal (0.164) Cardiovascular (0.115) Hematopoietic/Immune (0.115)	Cancer (0.443) Inflammation (0.442) Fetal (0.197)	pINCY
95	Reproductive (0.333) Cardiovascular (0.167) Gastrointestinal (0.167)	Cancer (0.750) Inflammation (0.250)	pINCY
96	Reproductive (0.369) Nervous (0.215) Hematopoietic/Immune (0.108) Gastrointestinal (0.108)	Cancer (0.508) Inflammation (0.231) Fetal (0.108)	pBLUESCRIPT
97	Reproductive (0.321) Gastrointestinal (0.179) Hematopoietic/Immune (0.161)	Inflammation (0.411) Cancer (0.393) Fetal (0.161)	pINCY
98	Reproductive (0.205) Nervous (0.192) Cardiovascular (0.164)	Cancer (0.452) Inflammation (0.342) Fetal (0.178)	pSPORT1

TABLE 3 cont.

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
99	Gastrointestinal (0.423) Reproductive (0.115)	Cancer (0.385) Inflammation (0.288) Fetal (0.173)	pSPORT1
100	Reproductive (0.281) Hematopoietic/Immune (0.234) Nervous (0.141)	Cancer (0.375) Fetal (0.312) Inflammation (0.312)	pINCY
101	Reproductive (0.294) Nervous (0.196) Gastrointestinal (0.118)	Cancer (0.529) Fetal (0.255)	pINCY
102	Reproductive (0.217) Nervous (0.163) Cardiovascular (0.141)	Cancer (0.435) Inflammation (0.174) Fetal (0.152)	pINCY
103	Reproductive (0.263) Hematopoietic/Immune (0.158) Musculoskeletal (0.158)	Cancer (0.526) Inflammation (0.263) Fetal (0.158)	pINCY
104	Nervous (0.400) Reproductive (0.300)	Cancer (0.400) Inflammation (0.300)	pSPORT1
105	Reproductive (0.375) Cardiovascular (0.125) Urologic (0.125)	Cancer (0.500) Inflammation (0.250) Fetal (0.208)	pINCY
106	Gastrointestinal (0.400) Reproductive (0.400) Developmental (0.100) Hematopoietic/Immune (0.100)	Cancer (0.600) Fetal (0.200) Inflammation (0.200)	pINCY
107	Reproductive (0.278) Gastrointestinal (0.152) Nervous (0.139)	Cancer (0.418) Inflammation (0.241) Fetal (0.165)	>pINCY
108	Reproductive (0.364) Hematopoietic/Immune (0.182) Nervous (0.167)	Inflammation (0.409) Cancer (0.364) Fetal (0.136)	pSPORT1

TABLE 3 cont.

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
109	Nervous (0.227) Reproductive (0.205) Cardiovascular (0.136) Urologic (0.136) Gastrointestinal (0.136)	Cancer (0.568) Inflammation (0.182) Fetal (0.136)	pINCY
110	Hematopoietic/Immune (0.400) Urologic (0.400) Reproductive (0.200)	Cell proliferation (0.800) Inflammation (0.800)	pBluescript
111	Gastrointestinal (0.213) Hematopoietic/Immune (0.191) Nervous (0.191)	Cell proliferation (0.744) Inflammation (0.489)	pBluescript
112	Hematopoietic/Immune (0.405) Gastrointestinal (0.167) Cardiovascular (0.119)	Inflammation (0.619) Cell proliferation (0.381)	pBluescript
113	Hematopoietic/Immune (0.667) Cardiovascular (0.333)	Inflammation (1.000)	pSPORT1
114	Cardiovascular (0.412) Nervous (0.235) Musculoskeletal (0.118)	Cell proliferation (0.765) Inflammation (0.353)	pSPORT1
115	Cardiovascular (0.548) Reproductive (0.161) Developmental (0.129)	Cell proliferation (0.806) Inflammation (0.226)	pINCY
116	Reproductive (0.267) Cardiovascular (0.233) Hematopoietic/Immune (0.233)	Cell proliferation (0.467) Inflammation (0.500)	pINCY
117	Reproductive (0.400) Cardiovascular (0.167) Gastrointestinal (0.133)	Cell proliferation (0.600) Inflammation (0.267)	pINCY
118	Nervous (0.205) Reproductive (0.205) Other (0.154)	Cell proliferation (0.461) Inflammation (0.385)	pINCY
119	Reproductive (0.500) Nervous (0.167) Hematopoietic/Immune (0.167)	Cancer (0.500) Inflammation (0.167) Neurological (0.167)	pINCY

TABLE 3 cont.

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
120	Reproductive (0.396) Cardiovascular (0.125) Musculoskeletal (0.125)	Cell proliferation (0.750) Inflammation (0.209)	pINCY
121	Reproductive (0.248) Hematopoietic/Immune (0.194) Gastrointestinal (0.147)	Cell Proliferation (0.651) Inflammation (0.380)	pINCY
122	Nervous (0.264) Cardiovascular (0.132) Reproductive (0.132)	Cell proliferation (0.547) Inflammation (0.396)	pINCY
123	Reproductive (0.242) Nervous (0.152) Urologic (0.152)	Cell proliferation (0.788) Inflammation (0.303)	pINCY
124	Nervous (0.333) Cardiovascular (0.167) Hematopoietic/Immune (0.167)	Cell proliferation (0.667) Inflammation (0.500)	pSPORT1
125	Reproductive (0.290) Cardiovascular (0.161) Hematopoietic/Immune (0.113)	Cell proliferation (0.709) Inflammation (0.306)	pSPORT1
126	Reproductive (0.360) Nervous (0.120) Urologic (0.100)	Cell proliferation (0.680) Inflammation (0.320)	pINCY
127	Reproductive (0.364) Gastrointestinal (0.145) Nervous (0.145)	Cell proliferation (0.600) Inflammation (0.400)	pINCY
128	Cardiovascular (0.154) Gastrointestinal (0.154) Reproductive (0.154)	Cell proliferation (0.616) Inflammation (0.308)	pINCY
129	Urologic (1.000)	Cancer (1.000)	pINCY
130	Hematopoietic/Immune (0.214) Cardiovascular (0.143) Gastrointestinal (0.143)	Cell proliferation (0.428) Inflammation (0.357)	pINCY

TABLE 4

Protein SEQ ID NO:	Clone ID	Library	Library Comment
1	001106	U937NOT01	U937NOT01 Library was constructed at Stratagene (STR937207) using RNA isolated from U937 monocyte-like cell line (ATCC CRL1593) established from malignant cells obtained from the pleural effusion of a 37-year-old Caucasian male with diffuse histiocytic lymphoma.
2	004586	HMC1NOT01	HMC1NOT01 Library was constructed using RNA isolated from HMC-1 human mast cell line derived from a 52-year-old female. Patient history included mast cell leukemia. Family history included atherosclerotic coronary artery disease, a joint disorder involving multiple joints, cerebrovascular disease, and diabetes insipidus.
3	052927	FIBRNOT01	FIBRNOT01 Library was constructed at Stratagene (STR937212) using RNA isolated from the WI38 lung fibroblast cell line derived from a 3-month-old Caucasian female fetus.
4	082843	HUVESTB01	HUVESTB01 Library was constructed using RNA isolated from shear-stressed HUV-EC-C (ATCC CRL 1730), an endothelial cell line derived from the vein of a normal human umbilical.
5	322349	EOSIHET02	EOSIHET02 Library was constructed using RNA isolated from peripheral blood cells apheresed from a 48-year-old Caucasian male. Patient history included hyperesinophilia.
6	397663	PITUNOT02	PITUNOT02 Library was constructed using RNA (Clontech 6584-1) isolated from the pituitary gland of 87 male and female donors, 15 to 75 years old.
7	673766	CRBLNOT01	CRBLNOT01 Library was constructed using RNA isolated from cerebellum tissue of a 69-year-old Caucasian male, who died from chronic obstructive pulmonary disease. Patient history included heart failure, myocardial infarction, hypertension, osteoarthritis, and tobacco use.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
8	1504753	BRAITUT07	BRAITUT07 Library was constructed using RNA isolated from left frontal lobe tumor tissue removed from the brain of a 32-year-old Caucasian male during excision of a cerebral meningeal lesion. Pathology indicated low grade desmoplastic neuronal neoplasm. Family history included atherosclerotic coronary artery disease.
9	1760185	PITUNOT03	PITUNOT03 Library was constructed using RNA isolated from pituitary tissue of a 46-year-old Caucasian male who died from colon cancer. Patient history included arthritis and peptic ulcer disease.
10	1805061	SINTNOT13	SINTNOT13 Library was constructed using RNA isolated from ileum tissue removed from a 25-year-old Asian female during a partial colectomy and temporary ileostomy. Pathology indicated moderately active chronic ulcerative colitis involving colonic mucosa from the distal margin to the ascending colon. Family history included hyperlipidemia, depressive disorder, malignant cervical neoplasm, and viral hepatitis A.
11 12	1850120 1852290	LUNGFET03 LUNGFET03	LUNGFET03 Library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus who died at 20 weeks' gestation. The mother was given seven days of erythromycin treatment for bronchitis during the first trimester.
13	1944530	PITUNOT01	PITUNOT01 Library was constructed using RNA (Clontech 6584-2) isolated from the normal pituitary glands of 18 male and female Caucasian donors, 16 to 70 years old, who died from trauma.
14	2019742	CONNNOT01	CONNNOT01 Library was constructed using RNA isolated from mesentery fat tissue removed from a 71-year-old Caucasian male during a partial colectomy and permanent colostomy. Patient history included a cholecystectomy, viral hepatitis, and a hemangioma. Family history included atherosclerotic coronary artery disease, myocardial infarction, and extrinsic asthma.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
15	2056042	BEPINOT01	BEPINOT01 Library was constructed using RNA isolated from a bronchial epithelium (NHBE) primary cell line derived from a 54-year-old Caucasian male.
16	2398682	THP1AZT01	THP1AZT01 Library was constructed using RNA isolated from THP-1 promonocyte cells treated for three days with 0.8 micromolar 5-aza-2'-deoxycytidine. THP-1 (ATCC TIB 202) is a human promonocyte line derived from peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia.
17	2518753	BRAITUT21	BRAITUT21 Library was constructed using RNA isolated from brain tumor tissue removed from the midline frontal lobe of a 61-year-old Caucasian female during excision of a cerebral meningeal lesion. Pathology indicated subfrontal meningotheial meningioma with no atypia. Patient history included depressive disorder; family history included cerebrovascular disease, senile dementia, hyperlipidemia, benign hypertension, atherosclerotic coronary artery disease, and congestive heart failure.
18	2709055	PONSAZT01	PONSAZT01 Library was constructed using polyA RNA isolated from diseased pons tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.
19	2724537	LUNGTUT10	LUNGTUT10 Library was constructed using RNA isolated from lung tumor tissue removed from the left upper lobe of a 65-year-old Caucasian female during a segmental lung resection. Pathology indicated a metastatic grade 2 myxoid liposarcoma and metastatic grade 4 liposarcoma. Patient history included soft tissue cancer, breast cancer, and secondary lung cancer. Family history included benign hypertension.
20	025818	SPLNFET01	SPLNFET01 Library was constructed at Stratagene using RNA isolated from a pool of fetal spleen tissue. 2x10 ⁶ primary clones were amplified to stabilize the library for long-term storage. Amplification may significantly skew sequence abundances.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
21	438283	THYRN0T01	THYRN0T01 Library was constructed using RNA isolated from thyroid tissue removed from a 64-year-old Caucasian female who died from congestive heart failure.
22	619699	PGANN0T01	PGANN0T01 Library was constructed using RNA isolated from paraganglionic tumor tissue removed from the intra-abdominal region of a 46-year-old Caucasian male during exploratory laparotomy. Pathology indicated a benign paraganglioma and was associated with a grade 2 renal cell carcinoma, clear cell type, which did not penetrate the capsule. Surgical margins were negative for tumor.
23	693452	SYNORAT03	SYNORAT03 Library was constructed using RNA isolated from the wrist synovial membrane tissue of a 56-year-old female with rheumatoid arthritis.
24	839651	PROSTUT05	PROSTUT05 Library was constructed using RNA isolated from prostate tumor tissue removed from a 69-year-old Caucasian male during a radical prostatectomy. Pathology indicated adenocarcinoma (Gleason grade 3+4). Adenofibromatous hyperplasia was also present. Family history included congestive heart failure, multiple myeloma, hyperlipidemia, and rheumatoid arthritis.
25	1253545	LUNGFET03	LUNGFET03 Library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus who died at 20 weeks' gestation.
26	1425691	BEPINON01	BEPINON01 normalized bronchial epithelium library was constructed from 5.12 million independent clones from the BEPINOT01 library. RNA was made from a bronchial epithelium primary cell line derived from a 54-year-old Caucasian male. The normalization and hybridization conditions were adapted from Soares et al., PNAS (1994) 91:9228, using a longer (24-hour) reannealing hybridization period.
27	1484257	CORPNOT02	CORPNOT02 Library was constructed using RNA isolated from diseased corpus callosum tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
28	1732368	BRSTTUT08	BRSTTUT08 Library was constructed using RNA isolated from breast tumor tissue removed from a 45-year-old Caucasian female during unilateral extended simple mastectomy. Pathology indicated invasive nuclear grade 2-3 adenocarcinoma, ductal type, with 3 of 23 lymph nodes positive for metastatic disease. Greater than 50% of the tumor volume was in situ, both comedo and non-comedo types. Immunostains were positive for estrogen/progesterone receptors, and uninvolved tissue showed proliferative changes. The patient concurrently underwent a total abdominal hysterectomy. Patient history included valvuloplasty of mitral valve without replacement, rheumatic mitral insufficiency, and rheumatic heart disease. Family history included acute myocardial infarction, atherosclerotic coronary artery disease, and type II diabetes.
29	1870914	SKINBIT01	SKINBIT01 Library was constructed using RNA isolated from diseased skin tissue of the left lower leg. Patient history included erythema nodosum of the left lower leg.
30	1910984	CONNTUT01	CONNTUT01 Library was constructed using RNA isolated from a soft tissue tumor removed from the clival area of the skull of a 30-year-old Caucasian female. Pathology indicated chondroid chordoma with neoplastic cells reactive for keratin.
31	1943040	HIPONOT01	HIPONOT01 Library was constructed using RNA isolated from the hippocampus tissue of a 72-year-old Caucasian female who died from an intracranial bleed. Patient history included nose cancer, hypertension, and arthritis.
32	2076520	ISLTNOT01	ISLTNOT01 Library was constructed using RNA isolated from a pooled collection of pancreatic islet cells.
33	2291241	BRAINON01	BRAINON01 Library was constructed and normalized from 4.88 million independent clones from the BRAINOT03 library. RNA was made from brain tissue removed from a 26-year-old Caucasian male during cranioplasty and excision of a cerebral meningeal lesion. Pathology for the associated tumor tissue indicated a grade 4 oligoastrocytoma in the right fronto-parietal part of the brain.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
34	2329692	COLNNOT11	COLNNOT11 The COLNNOT11 library was constructed using RNA isolated from colon tissue removed from a 60-year-old Caucasian male during a left hemicolectomy.
35	2474110	THP1NOT03	THP1NOT03 Library was constructed using RNA isolated from untreated THP-1 cells (ATCC TIB 202), a human promonocyte line derived from the peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia.
36	2495790	ADRETUT05	ADRETUT05 Library was constructed using RNA isolated from adrenal tumor tissue removed from a 52-year-old Caucasian female during a unilateral adrenalectomy. Pathology indicated a pheochromocytoma.
37	2661254	ADRENOT08	ADRENOT08 pINCY Library was constructed using RNA isolated from adrenal tissue removed from a 20-year-old Caucasian male, who died from head trauma.
38	2674047	KIDNNOT19	KIDNNOT19 pINCY Library was constructed using RNA isolated from kidney tissue removed a 65-year-old Caucasian male during an exploratory laparotomy and nephroureterectomy. Pathology for the associated tumor tissue indicated a grade 1 renal cell carcinoma within the upper pole of the left kidney. Patient history included malignant melanoma of the abdominal skin, benign neoplasm of colon, cerebrovascular disease, and umbilical hernia. Family history included cardiovascular and cerebrovascular disease, and prostate cancer.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
39	2762174	BRAINOS12	BRAINOS12 pSPORT1 Library was constructed from 4.9 million clones from the BRAINOT03 library by subtraction of abundantly expressed clone pools. RNA was made from brain tissue removed from a 26-year-old Caucasian male during cranioplasty and excision of a cerebral meningeal lesion. Pathology for the associated tumor tissue indicated a grade 4 oligoastrocytoma in the right fronto-parietal part of the brain.
40	2765991	BRSTNOT12	BRSTNOT12 pINCY Library was constructed using RNA isolated from diseased breast tissue removed from a 32-year-old Caucasian female during a bilateral reduction mammoplasty. Pathology indicated nonproliferative fibrocystic disease. Family history included benign hypertension and atherosclerotic coronary artery disease.
41	2775157	PANCNOT15	PANCNOT15 pINCY Library was constructed using RNA isolated from diseased pancreatic tissue removed from a 15-year-old Caucasian male during a exploratory laparotomy with distal pancreatectomy and total splenectomy. Pathology indicated islet cell hyperplasia. Family history included prostate cancer and cardiovascular disease.
42	2918375	THYMFET03	THYMFET03 Library was constructed using RNA isolated from thymus tissue removed from a Caucasian male fetus.
43	3149729	ADRENON04	ADRENON04 normalized adrenal gland library was constructed from 1.36 million independent clones from an adrenal tissue library. Starting RNA was made from adrenal gland tissue removed from a 20-year-old Caucasian male who died from head trauma. The library was normalized in two rounds using conditions adapted from Soares et al. (PNAS (1994) 91:9228-9232) and Bonaldo et al. (Genome Res (1996) 6: 791-806) and a significantly longer (48-hours/round) reannealing hybridization period.
44	3705895	PENCNOT07	PENCNOT07 Library was constructed using RNA isolated from penis right corpora cavernosa tissue removed from a male.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
45	003256	HMC1NOT01	HMC1NOT01 library was constructed using RNA isolated from the HMC-1 human mast cell line derived from a 52-year-old female. Patient history included mast cell leukemia.
46	156986	THP1PLB02	THP1PLB02 library was constructed by reamplification of THP1PLB01, which was made using RNA isolated from THP-1 cells cultured for 48 hours with 100 ng/ml phorbol ester (PMA), followed by a 4-hour culture in media containing 1 ug/ml LPS. THP-1 (ATCC TIB 202) is a human promonocyte line derived from the peripheral blood of a 1-year-old male with acute monocytic leukemia (ref: Int. J. Cancer (1980) 26:171).
47	319415	EOSIHET02	EOSIHET02 library was constructed using RNA isolated from peripheral blood cells adhered from a 48-year-old Caucasian male. Patient history included hypereosinophilia. The cell population was determined to be greater than 77% eosinophils by Wright's staining.
48	635581	NEUTGMT01	NEUTGMT01 library was constructed using RNA isolated from peripheral blood granulocytes collected by density gradient centrifugation through Ficoll-Hypaque. The cells were isolated from buffy coat units obtained from 20 unrelated male and female donors. Cells were cultured in 10 nM GM-CSF for 1 hour before washing and harvesting for total RNA preparation.
49	921803	RATRN0T02	RATRN0T02 library was constructed using RNA isolated from the right atrium tissue of a 39-year-old Caucasian male, who died from a gunshot wound.
50	1250492	LUNGFET03	LUNGFET03 library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus, who died at 20 weeks' gestation.
51	1427838	SINTBST01	SINTBST01 library was constructed using RNA isolated from ileum tissue obtained from an 18-year-old Caucasian female during bowel anastomosis. Pathology indicated Crohn's disease of the ileum, involving 15 cm of the small bowel. Family history included cerebrovascular disease and atherosclerotic coronary artery disease.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
52	1448258	PLACNOT02	PLACNOT02 library was constructed using RNA isolated from the placental tissue of a Hispanic female fetus, who was prematurely delivered at 21 weeks' gestation. Serologies of the mother's blood were positive for CMV (cytomegalovirus).
53	1645941	PROSTUT09	PROSTUT09 library was constructed using RNA isolated from prostate tumor tissue removed from a 66-year-old Caucasian male during a radical prostatectomy, radical cystectomy, and urinary diversion. Pathology indicated grade 3 transitional cell carcinoma. The patient presented with prostatic inflammatory disease. Patient history included lung neoplasm and benign hypertension. Family history included a malignant breast neoplasm, tuberculosis, cerebrovascular disease, atherosclerotic coronary artery disease and lung cancer.
54	1646005	PROSTUT09	PROSTUT09 library was constructed using RNA isolated from prostate tumor tissue removed from a 66-year-old Caucasian male during a radical prostatectomy, radical cystectomy, and urinary diversion. Pathology indicated grade 3 transitional cell carcinoma. The patient presented with prostatic inflammatory disease. Patient history included lung neoplasm and benign hypertension. Family history included a malignant breast neoplasm, tuberculosis, cerebrovascular disease, atherosclerotic coronary artery disease and lung cancer.
55	1686561	PROSNOT15	PROSNOT15 library was constructed using RNA isolated from diseased prostate tissue removed from a 66-year-old Caucasian male during radical prostatectomy and regional lymph node excision. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated an adenocarcinoma (Gleason grade 2+3). The patient presented with elevated prostate specific antigen (PSA). Family history included prostate cancer, secondary bone cancer, and benign hypertension.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
56	1821233	GBLATUT01	The GBLATUT01 library was constructed using RNA isolated from gallbladder tumor tissue removed from a 78-year-old Caucasian female during a cholecystectomy. Pathology indicated invasive grade 2 squamous cell carcinoma, forming a mass in the gallbladder. Patient history included diverticulitis of the colon, palpitations, benign hypertension, and hyperlipidemia. Family history included a cholecystectomy, atherosclerotic coronary artery disease, atherosclerotic coronary artery disease, hyperlipidemia, and benign hypertension.
57	1877278	LEUKNOT03	The LEUKNOT03 library was constructed using RNA isolated from white blood cells of a 27-year-old female with blood type A+. The donor tested negative for cytomegalovirus (CMV).
58	1880692	LEUKNOT03	The LEUKNOT03 library was constructed using RNA isolated from white blood cells of a 27-year-old female with blood type A+. The donor tested negative for cytomegalovirus (CMV).
59	2280456	PROSNON01	The PROSNON01 library was constructed and normalized from 4.4 Million independent clones from the PROSNOT11 library. RNA was made from prostate tissue removed from a 28-year-old Caucasian male who died from a self-inflicted gunshot wound. The normalization and hybridization conditions were adapted from Soares, M.B. et al. (1994) Proc. Natl. Acad. Sci. USA 91:9228-9232, using a longer (19 hour) reannealing hybridization period.
60	2284580	BRAINON01	The BRAINON01 library was constructed and normalized from 4.88 million independent clones from the BRAINOT03 library. RNA was made from brain tissue removed from a 26-year-old Caucasian male during cranioplasty and excision of a cerebral meningeal lesion. Pathology for the associated tumor tissue indicated a grade 4 oligoastrocytoma in the right fronto-parietal part of the brain.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
61	2779172	OVARTUT03	OVARTUT03 library was constructed using RNA isolated from ovarian tumor tissue removed from the left ovary of a 52-year-old mixed ethnicity female during a total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal and lymphatic structure biopsy, regional lymph node excision, and peritoneal tissue destruction. Pathology indicated an invasive grade 3 (of 4) seroanaplastic carcinoma forming a mass in the left ovary. Patient history included breast cancer, chronic peptic ulcer, and joint pain. Family history included colon cancer, cerebrovascular disease, breast cancer, type II diabetes, esophagus cancer, and depressive disorder.
62	3279329	STOMFET02	STOMFET02 library was constructed using RNA isolated from stomach tissue removed from a Hispanic male fetus, who died at 18 weeks' gestation.
63	3340290	SPLNNOT10	SPLNNOT10 library was constructed using RNA isolated from spleen tissue removed from a 59-year-old Caucasian male during a total splenectomy and exploratory laparotomy. Pathology for the spleen indicated splenomegaly with congestion. The lymph nodes showed reactive follicular hyperplasia. The liver showed mild, nonspecific steatosis. The patient presented with abdominal pain, bloating of the abdomen, low-grade fever, and diaphoresis. Family history included myocardial infarction, arteriosclerotic cardiovascular disease, primary tuberculous infection, cerebrovascular disease and lymphoma.
64	3376404	PENGNOT01	PENGNOT01 library was constructed using RNA isolated from glans tissue removed from the penis of a 3-year-old Black male. Pathology for the associated tumor tissue indicated invasive grade 4 urothelial carcinoma forming a soft tissue scrotal mass that invaded the cavernous body of the penis and encased both testicles.
65	4173111	SINTNOT21	SINTNOT21 library was constructed using RNA isolated from small intestine tissue obtained from a 8-year-old Black male, who died from anoxia. Serology was negative.

Table 5

Program	Description	Reference	Parameter Threshold
ABI FACTURA	A program that removes vector sequences and masks ambiguous bases in nucleic acid sequences.	Perkin-Elmer Applied Biosystems, Foster City, CA.	
ABI/PARACEL FDF	A Fast Data Finder useful in comparing and annotating amino acid or nucleic acid sequences.	Perkin-Elmer Applied Biosystems, Foster City, CA; Paracel Inc., Pasadena, CA.	Mismatch <50%
ABI AutoAssembler	A program that assembles nucleic acid sequences.	Perkin-Elmer Applied Biosystems, Foster City, CA.	
BLAST	A Basic Local Alignment Search Tool useful in sequence similarity search for amino acid and nucleic acid sequences. BLAST includes five functions: blastp, blastn, blastx, tblastn, and tblastx.	Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410; Altschul, S.F. et al. (1997) Nucleic Acids Res. 25: 3389-3402.	ESTs: Probability value= 1.0E-8 or less Full Length sequences: Probability value= 1.0E-10 or less
FASTA	A Pearson and Lipman algorithm that searches for similarity between a query sequence and a group of sequences of the same type. FASTA comprises as least five functions: fasta, tfasta, fastx, tfastx, and ssearch.	Pearson, W.R. and D.J. Lipman (1988) Proc. Natl. Acad. Sci. 85:2444-2448; Pearson, W.R. (1990) Methods Enzymol. 183: 63-98; and Smith, T.F. and M. S. Waterman (1981) Adv. Appl. Math. 2:482-489.	ESTs: fasta E value=1.06E-6 Assembled ESTs: fasta Identity= 95% or greater and Match length=200 bases or greater; fastx E value=1.0E-8 or less Full Length sequences: fastx score=100 or greater
BLIMPS	A BLOCKS IMPROVED Searcher that matches a sequence against those in BLOCKS, PRINTS, DOMO, PRODOM, and PFAM databases to search for gene families, sequence homology, and structural fingerprint regions.	Henikoff, S and J.G. Henikoff, Nucl. Acid Res., 19:6565-72, 1991. J.G. Henikoff and S. Henikoff (1996) Methods Enzymol. 266:88-105; and Attwood, T.K. et al. (1997) J. Chem. Inf. Comput. Sci. 37: 417-424.	Score=1000 or greater; Ratio of Score/Strength = 0.75 or larger; and, if applicable, Probability value= 1.0E-3 or less
HMMER	An algorithm for searching a query sequence against hidden Markov model (HMM)-based databases of protein family consensus sequences, such as PFAM.	Krogh, A. et al. (1994) J. Mol. Biol., 235:1501-1531; Sonnhammer, E.L.L. et al. (1988) Nucleic Acids Res. 26:320-322.	Score=10-50 bits for PFAM hits, depending on individual protein families

Table 5 cont.

Program	Description	Reference	Parameter Threshold
ProfileScan	An algorithm that searches for structural and sequence motifs in protein sequences that match sequence patterns defined in Prosite.	Gribskov, M. et al. (1988) CABIOS 4:61-66; Gribskov, et al. (1989) Methods Enzymol. 183:146-159; Bairoch, A. et al. (1997) Nucleic Acids Res. 25: 217-221.	Score= 4.0 or greater
Phred	A base-calling algorithm that examines automated sequencer traces with high sensitivity and probability.	Ewing, B. et al. (1998) Genome Res. 8:175-185; Ewing, B. and P. Green (1998) Genome Res. 8:186-194.	
Phrap	A Phils Revised Assembly Program including SWAT and CrossMatch, programs based on efficient implementation of the Smith-Waterman algorithm, useful in searching sequence homology and assembling DNA sequences.	Smith, T.F. and M. S. Waterman (1981) Adv. Appl. Math. 2:482-489; Smith, T.F. and M. S. Waterman (1981) J. Mol. Biol. 147:195-197; and Green, P., University of Washington, Seattle, WA.	Score= 120 or greater; Match length= 56 or greater
Consed	A graphical tool for viewing and editing Phrap assemblies	Gordon, D. et al. (1998) Genome Res. 8:195-202.	
SPScan	A weight matrix analysis program that scans protein sequences for the presence of secretory signal peptides.	Nielson, H. et al. (1997) Protein Engineering 10:1-6; Claverie, J.M. and S. Audic (1997) CABIOS 12: 431-439.	Score=5 or greater
Motifs	A program that searches amino acid sequences for patterns that matched those defined in Prosite.	Bairoch et al. <i>supra</i> ; Wisconsin Package Program Manual, version 9, page M51-59, Genetics Computer Group, Madison, WI.	

What is claimed is:

1. A substantially purified polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof.
- 5 2. A substantially purified variant having at least 90% amino acid sequence identity to the amino acid sequence of claim 1.
3. An isolated and purified polynucleotide encoding the polypeptide of claim 1.
4. An isolated and purified polynucleotide variant having at least 70% polynucleotide sequence identity to the polynucleotide of claim 3.
- 10 5. An isolated and purified polynucleotide which hybridizes under stringent conditions to the polynucleotide of claim 3.
6. An isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide of claim 3.
7. A method for detecting a polynucleotide, the method comprising the steps of:
 - 15 (a) hybridizing the polynucleotide of claim 6 to at least one nucleic acid in a sample, thereby forming a hybridization complex; and
 - (b) detecting the hybridization complex, wherein the presence of the hybridization complex correlates with the presence of the polynucleotide in the sample.
8. The method of claim 7 further comprising amplifying the polynucleotide prior to
20 hybridization.
9. An isolated and purified polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:66-130, and fragments thereof.
10. An isolated and purified polynucleotide variant having at least 70% polynucleotide sequence identity to the polynucleotide of claim 9.
- 25 11. An isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide of claim 9.
12. An expression vector comprising at least a fragment of the polynucleotide of claim 3.
13. A host cell comprising the expression vector of claim 12.
- 30 14. A method for producing a polypeptide, the method comprising the steps of:
 - a) culturing the host cell of claim 13 under conditions suitable for the expression of the polypeptide; and
 - b) recovering the polypeptide from the host cell culture.
15. A pharmaceutical composition comprising the polypeptide of claim 1 in
35 conjunction with a suitable pharmaceutical carrier.

16. A purified antibody which specifically binds to the polypeptide of claim 1.
17. A purified agonist of the polypeptide of claim 1.
18. A purified antagonist of the polypeptide of claim 1.
19. A method for treating or preventing a disorder associated with decreased
5 expression or activity of HTRM, the method comprising administering to a subject in need of such
treatment an effective amount of the pharmaceutical composition of claim 15.
20. A method for treating or preventing a disorder associated with increased
expression or activity of HTRM, the method comprising administering to a subject in need of such
treatment an effective amount of the antagonist of claim 18.

SEQUENCE LISTING

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 HILLMAN, Jennifer L.
 BANDMAN, Olga
 LAL, Preeti
 YUE, Henry
 REDDY, Roopa
 TANG, Y. Tom
 GERSTIN, Edward H.
 PATTERSON, Chandra
 BAUGHN, Mariah R.
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Ala	Ser	Gly	Gly	Gly	Val	Val	Ala	Ile	Asp	Asn	Lys	Ile	Glu	Gln	60	65	70	75
Ala	Met	Asp	Leu	Val	Lys	Ser	His	Leu	Met	Tyr	Ala	Val	Arg	Glu	80	85	90	95
Glu	Val	Glu	Val	Leu	Lys	Glu	Gln	Ile	Lys	Glu	Leu	Val	Glu	Arg	100	105	110	115
Asn	Ser	Leu	Leu	Glu	Arg	Glu	Asn	Ala	Leu	Leu	Lys	Ser	Leu	Ser	120	125	130	135
Ser	Asn	Asp	Gln	Leu	Ser	Gln	Leu	Pro	Thr	Gln	Gln	Ala	Asn	Pro	140	145	150	155
Gly	Ser	Thr	Ser	Gln	Gln	Gln	Ala	Val	Ile	Ala	Gln	Pro	Pro	Gln	160	165	170	175

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135

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<220>  
<221> misc_feature  
<223> Incyte clone 1760185CD1
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```

<400> 9
Met Arg Pro Leu Asp Ile Val Glu Leu Ala Glu Pro Glu Glu Val
  1                    5                    10                    15
Glu Val Leu Glu Pro Glu Glu Asp Phe Glu Gln Phe Leu Leu Pro
                    20                    25                    30
Val Ile Asn Glu Met Arg Glu Asp Ile Ala Ser Leu Thr Arg Glu
                    35                    40                    45
His Gly Arg Ala Tyr Leu Arg Asn Arg Ser Lys Leu Trp Glu Met
                    50                    55                    60
Asp Asn Met Leu Ile Gln Ile Lys Thr Gln Val Glu Ala Ser Glu
                    65                    70                    75
Glu Ser Ala Leu Asn His Leu Gln Asn Pro Gly Asp Ala Ala Glu
                    80                    85                    90
Gly Arg Ala Ala Lys Arg Cys Glu Lys Ala Glu Glu Lys Ala Lys
                    95                    100                   105
Glu Ile Ala Lys Met Ala Glu Met Leu Val Glu Leu Val Arg Arg
                    110                   115                   120
Ile Glu Lys Ser Glu Ser Ser
                    125

```

```
<220>
<221> misc_feature
<223> incyte clone 1805061CD1
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<400>	10													
Met	Pro	Tyr	Val	Asp	Arg	Gln	Asn	Arg	Ile	Cys	Gly	Phe	Leu	Asp
1				5					10					15
Ile	Glu	Glu	Asn	Glu	Asn	Ser	Gly	Lys	Phe	Leu	Arg	Arg	Tyr	Phe
				20					25					30
Ile	Leu	Asp	Thr	Arg	Glu	Asp	Ser	Phe	Val	Trp	Tyr	Met	Asp	Asn
				35					40					45
Pro	Gln	Asn	Leu	Pro	Ser	Gly	Ser	Ser	Arg	Val	Gly	Ala	Ile	Lys
				50					55					60
Leu	Thr	Tyr	Ile	Ser	Lys	Val	Ser	Asp	Ala	Thr	Lys	Leu	Arg	Pro
				65					70					75
Lys	Ala	Glu	Phe	Cys	Phe	Val	Met	Asn	Ala	Gly	Met	Arg	Lys	Tyr
				80					85					90
Phe	Leu	Gln	Ala	Asn	Asp	Gln	Gln	Asp	Leu	Val	Glu	Trp	Val	Asn
				95					100					105

Val	Leu	Asn	Lys	Ala	Ile	Lys	Ile	Thr	Val	Pro	Lys	Gln	Ser	Asp	
				110					115					120	
Ser	Gln	Pro	Asn	Ser	Asp	Asn	Leu	Ser	Arg	His	Gly	Glu	Cys	Gly	
				125					130					135	
Lys	Lys	Gln	Val	Ser	Tyr	Arg	Thr	Asp	Ile	Val	Gly	Gly	Val	Pro	
				140					145					150	
Ile	Ile	Thr	Pro	Thr	Gln	Lys	Glu	Glu	Val	Asn	Glu	Cys	Gly	Glu	
				155					160					165	
Ser	Ile	Asp	Arg	Asn	Asn	Leu	Lys	Arg	Ser	Gln	Ser	His	Leu	Pro	
				170					175					180	
Tyr	Phe	Thr	Pro	Lys	Pro	Pro	Gln	Asp	Ser	Ala	Val	Ile	Lys	Ala	
				185					190					195	
Gly	Tyr	Cys	Val	Lys	Gln	Gly	Ala	Val	Met	Lys	Asn	Trp	Lys	Arg	
				200					205					210	
Arg	Tyr	Phe	Gln	Leu	Asp	Glu	Asn	Thr	Ile	Gly	Tyr	Phe	Lys	Ser	
				215					220					225	
Glu	Leu	Glu	Lys	Glu	Pro	Leu	Arg	Val	Ile	Pro	Leu	Lys	Glu	Val	
				230					235					240	
His	Lys	Val	Gln	Glu	Cys	Lys	Gln	Ser	Asp	Ile	Met	Met	Arg	Asp	
				245					250					255	
Asn	Leu	Phe	Glu	Ile	Val	Thr	Thr	Ser	Arg	Thr	Phe	Tyr	Val	Gln	
				260					265					270	
Ala	Asp	Ser	Pro	Glu	Glu	Met	His	Ser	Trp	Ile	Lys	Ala	Val	Ser	
				275					280					285	
Gly	Ala	Ile	Val	Ala	Gln	Arg	Gly	Pro	Gly	Arg	Ser	Ala	Ser	Ser	
				290					295					300	
Met	Arg	Gln	Ala	Arg	Arg	Leu	Ser	Asn	Pro	Cys	Ile	Gln	Arg	Ser	
				305					310					315	
Ile	Pro	Pro	Val	Leu	Gln	Asn	Pro	Asn	Thr	Leu	Ser	Val	Leu	Pro	
				320					325					330	
Thr	Gln	Pro	Pro	Pro	Pro	His	Ile	Pro	Gln	Pro	Leu	Ala	Ala	Thr	
				335					340					345	
Leu	Trp	Ser	Gln	Pro	Leu	Pro	Trp	Arg	Ser	Glu	Asp	Phe	Thr	Ser	
				350					355					360	
Leu	Leu	Pro	Arg	Ser	Ser	Gln	Gly	Thr	Ser	Arg	Ser	Arg	Leu	Ser	
				365					370					375	
Leu	Gln	Glu	Asn	Gln	Leu	Pro	Lys								
				380											

<210> 11

<211> 254

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1850120CD1

<400> 11

Met	Ser	Leu	Ala	Arg	Gly	His	Gly	Asp	Thr	Ala	Ala	Ser	Thr	Ala	
1				5					10					15	
Ala	Pro	Leu	Ser	Glu	Glu	Gly	Glu	Val	Thr	Ser	Gly	Leu	Gln	Ala	
				20					25					30	
Leu	Ala	Val	Glu	Asp	Thr	Gly	Gly	Pro	Ser	Ala	Ser	Ala	Gly	Lys	
				35					40					45	
Ala	Glu	Asp	Glu	Gly	Glu	Gly	Gly	Arg	Glu	Glu	Thr	Glu	Arg	Glu	
				50					55					60	
Gly	Ser	Gly	Gly	Glu	Glu	Ala	Gln	Gly	Glu	Val	Pro	Ser	Ala	Gly	
				65					70					75	
Gly	Glu	Glu	Pro	Ala	Glu	Glu	Asp	Ser	Glu	Asp	Trp	Cys	Val	Pro	
				80					85					90	
Cys	Ser	Asp	Glu	Glu	Val	Glu	Leu	Pro	Ala	Asp	Gly	Gln	Pro	Trp	
				95					100					105	

```

Met Pro Pro Pro Ser Glu Ile Gln Arg Leu Tyr Glu Leu Leu Ala
110 115 120
Ala His Gly Thr Leu Glu Leu Gln Ala Glu Ile Leu Pro Arg Arg
125 130 135
Pro Pro Thr Pro Glu Arg Gln Ser Glu Glu Glu Arg Ser Asp Glu
140 145 150
Glu Pro Glu Ala Lys Glu Glu Glu Glu Glu Lys Pro His Met Pro
155 160 165
Thr Glu Phe Asp Phe Asp Asp Glu Pro Val Thr Pro Lys Asp Ser
170 175 180
Leu Ile Asp Arg Arg Arg Thr Pro Gly Ser Ser Ala Arg Ser Gln
185 190 195
Lys Arg Glu Ala Arg Leu Asp Lys Val Leu Ser Asp Met Lys Arg
200 205 210
His Lys Lys Leu Glu Glu Gln Ile Leu Arg Thr Gly Arg Asp Leu
215 220 225
Phe Ser Leu Asp Ser Glu Asp Pro Ser Pro Ala Ser Pro Pro Leu
230 235 240
Arg Ser Ser Gly Ser Ser Leu Phe Pro Arg Gln Arg Lys Tyr
245 250

```

<210> 12

<211> 305

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<223> Incyte clone 1852290CD1

<400> 12

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Met Ala Leu Cys Ala Leu Thr Arg Ala Leu Arg Ser Leu Asn Leu
1 5 10 15
Ala Pro Pro Thr Val Ala Ala Pro Ala Pro Ser Leu Phe Pro Ala
20 25 30
Ala Gln Met Met Asn Asn Gly Leu Leu Gln Gln Pro Ser Ala Leu
35 40 45
Met Leu Leu Pro Cys Arg Pro Val Leu Thr Ser Val Ala Leu Asn
50 55 60
Ala Asn Phe Val Ser Trp Lys Ser Arg Thr Lys Tyr Thr Ile Thr
65 70 75
Pro Val Lys Met Arg Lys Ser Gly Gly Arg Asp His Thr Gly Arg
80 85 90
Ile Arg Val His Gly Ile Gly Gly Gly His Lys Gln Arg Tyr Arg
95 100 105
Met Ile Asp Phe Leu Arg Phe Arg Pro Glu Thr Lys Ser Gly
110 115 120
Pro Phe Glu Glu Lys Val Ile Gln Val Arg Tyr Asp Pro Cys Arg
125 130 135
Ser Ala Asp Ile Ala Leu Val Ala Gly Gly Ser Arg Lys Arg Trp
140 145 150
Ile Ile Ala Thr Glu Asn Met Gln Ala Gly Asp Thr Ile Leu Asn
155 160 165
Ser Asn His Ile Gly Arg Met Ala Val Ala Ala Arg Glu Gly Asp
170 175 180
Ala His Pro Leu Gly Ala Leu Pro Val Gly Thr Leu Ile Asn Asn
185 190 195
Val Glu Ser Glu Pro Gly Arg Gly Ala Gln Tyr Ile Arg Ala Ala
200 205 210
Gly Thr Cys Gly Val Leu Leu Arg Lys Val Asn Gly Thr Ala Ile
215 220 225

```

Ile	Gln	Leu	Pro	Ser	Lys	Arg	Gln	Met	Gln	Val	Leu	Glu	Thr	Cys
				230					235					240
Val	Ala	Thr	Val	Gly	Arg	Val	Ser	Asn	Val	Asp	His	Asn	Lys	Arg
				245					250					255
Val	Ile	Gly	Lys	Ala	Gly	Arg	Asn	Arg	Trp	Leu	Gly	Lys	Arg	Pro
				260					265					270
Asn	Ser	Gly	Arg	Trp	His	Arg	Lys	Gly	Gly	Trp	Ala	Gly	Arg	Lys
				275					280					285
Ile	Arg	Pro	Leu	Pro	Pro	Met	Lys	Ser	Tyr	Val	Lys	Leu	Pro	Ser
				290					295					300
Ala	Ser	Ala	Gln	Ser										
				305										

<210> 13

<211> 230

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1944530CD1

<400> 13

Met	Gly	Gln	Gln	Ile	Ser	Asp	Gln	Thr	Gln	Leu	Val	Ile	Asn	Lys
1				5					10					15
Leu	Pro	Glu	Lys	Val	Ala	Lys	His	Val	Thr	Leu	Val	Arg	Glu	Ser
				20					25					30
Gly	Ser	Leu	Thr	Tyr	Glu	Glu	Phe	Leu	Gly	Arg	Val	Ala	Glu	Leu
				35					40					45
Asn	Asp	Val	Thr	Ala	Lys	Val	Ala	Ser	Gly	Gln	Glu	Lys	His	Leu
				50					55					60
Leu	Phe	Glu	Val	Gln	Pro	Gly	Ser	Asp	Ser	Ser	Ala	Phe	Trp	Lys
				65					70					75
Val	Val	Val	Arg	Val	Val	Cys	Thr	Lys	Ile	Asn	Lys	Ser	Ser	Gly
				80					85					90
Ile	Val	Glu	Ala	Ser	Arg	Ile	Met	Asn	Leu	Tyr	Gln	Phe	Ile	Gln
				95					100					105
Leu	Tyr	Lys	Asp	Ile	Thr	Ser	Gln	Ala	Ala	Gly	Val	Leu	Ala	Gln
				110					115					120
Ser	Ser	Thr	Ser	Glu	Pro	Asp	Glu	Asn	Ser	Ser	Ser	Val	Thr	
				125					130					135
Ser	Cys	Gln	Ala	Ser	Leu	Trp	Met	Gly	Arg	Val	Lys	Gln	Leu	Thr
				140					145					150
Asp	Glu	Glu	Glu	Cys	Cys	Ile	Cys	Met	Asp	Gly	Arg	Ala	Asp	Leu
				155					160					165
Ile	Leu	Pro	Cys	Ala	His	Ser	Phe	Cys	Gln	Lys	Cys	Ile	Asp	Lys
				170					175					180
Trp	Ser	Asp	Arg	His	Arg	Asn	Cys	Pro	Ile	Cys	Arg	Leu	Gln	Met
				185					190					195
Thr	Gly	Ala	Asn	Glu	Ser	Trp	Val	Val	Ser	Asp	Ala	Pro	Thr	Glu
				200					205					210
Asp	Asp	Met	Ala	Asn	Tyr	Ile	Leu	Asn	Met	Ala	Asp	Glu	Ala	Gly
				215					220					225
Gln	Pro	His	Arg	Pro										
				230										

<210> 14

<211> 292

<212> PRT

<213> Homo sapiens

<220>

WO 99/57144

PCT/US99/09935

<221> misc_feature

<223> Incyte clone 2019742CB1

<400> 14

```

Met Ser Gly Met Glu Ala Thr Val Thr Ile Pro Ile Trp Gln Asn
 1          5          10          15
Lys Pro His Gly Ala Ala Arg Ser Val Val Arg Arg Ile Gly Thr
          20          25          30
Asn Leu Pro Leu Lys Pro Cys Ala Arg Ala Ser Phe Glu Thr Leu
          35          40          45
Pro Asn Ile Ser Asp Leu Cys Leu Arg Asp Val Pro Pro Val Pro
          50          55          60
Thr Leu Ala Asp Ile Ala Trp Ile Ala Ala Asp Glu Glu Glu Thr
          65          70          75
Tyr Ala Arg Val Arg Ser Asp Thr Arg Pro Leu Arg His Thr Trp
          80          85          90
Lys Pro Ser Pro Leu Ile Val Met Gln Arg Asn Ala Ser Val Pro
          95          100          105
Asn Leu Arg Gly Ser Glu Glu Arg Leu Leu Ala Leu Lys Lys Pro
          110          115          120
Ala Leu Pro Ala Leu Ser Arg Thr Thr Glu Leu Gln Asp Glu Leu
          125          130          135
Ser His Leu Arg Ser Gln Ile Ala Lys Ile Val Ala Ala Asp Ala
          140          145          150
Ala Ser Ala Ser Leu Thr Pro Asp Phe Leu Ser Pro Gly Ser Ser
          155          160          165
Asn Val Ser Ser Pro Leu Pro Cys Phe Gly Ser Ser Phe His Ser
          170          175          180
Thr Thr Ser Phe Val Ile Ser Asp Ile Thr Glu Glu Thr Glu Val
          185          190          195
Glu Val Pro Glu Leu Pro Ser Val Pro Leu Leu Cys Ser Ala Ser
          200          205          210
Pro Glu Cys Cys Lys Pro Glu His Lys Ala Ala Cys Ser Ser Ser
          215          220          225
Glu Glu Asp Asp Cys Val Ser Leu Ser Lys Ala Ser Ser Phe Ala
          230          235          240
Asp Met Met Gly Ile Leu Lys Asp Phe His Arg Met Lys Gln Ser
          245          250          255
Gln Asp Leu Asn Arg Ser Leu Leu Lys Glu Glu Asp Pro Ala Val
          260          265          270
Leu Ile Ser Glu Val Leu Arg Arg Lys Phe Ala Leu Lys Glu Glu
          275          280          285
Asp Ile Ser Arg Lys Gly Asn
          290

```

<210> 15

<211> 232

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2056042CD1

<400> 15

```

Met Ala Ser Ser Ala Ala Ser Ser Glu His Phe Glu Lys Leu His
 1          5          10          15
Glu Ile Phe Arg Gly Leu His Glu Asp Leu Gln Gly Val Pro Glu
          20          25          30
Arg Leu Leu Gly Thr Ala Gly Thr Glu Glu Lys Lys Lys Leu Ile
          35          40          45
Arg Asp Phe Asp Glu Lys Gln Gln Glu Ala Asn Glu Thr Leu Ala
          50          55          60

```

```

Glu Met Glu Glu Glu Leu Arg Tyr Ala Pro Leu Ser Phe Arg Asn
      65              70              75
Pro Met Met Ser Lys Leu Arg Asn Tyr Arg Lys Asp Leu Ala Lys
      80              85              90
Leu His Arg Glu Val Arg Ser Thr Pro Leu Thr Ala Thr Pro Gly
      95              100             105
Gly Arg Gly Asp Met Lys Tyr Gly Ile Tyr Ala Val Glu Asn Glu
      110             115             120
His Met Asn Arg Leu Gln Ser Gln Arg Ala Met Leu Leu Gln Gly
      125             130             135
Thr Glu Ser Leu Asn Arg Ala Thr Gln Ser Ile Glu Arg Ser His
      140             145             150
Arg Ile Ala Thr Glu Thr Asp Gln Ile Gly Ser Glu Ile Ile Glu
      155             160             165
Glu Leu Gly Glu Gln Arg Asp Gln Leu Glu Arg Thr Lys Ser Arg
      170             175             180
Leu Val Asn Thr Ser Glu Asn Leu Ser Lys Ser Arg Lys Ile Leu
      185             190             195
Arg Ser Met Ser Arg Lys Val Thr Thr Asn Lys Leu Leu Leu Ser
      200             205             210
Ile Ile Ile Leu Leu Glu Leu Ala Ile Leu Gly Gly Leu Val Tyr
      215             220             225
Tyr Lys Phe Phe Arg Ser His
      230

```

```

<210> 16
<211> 376
<212> PRT
<213> Homo sapiens

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```

<220>
<221> misc_feature
<223> Incyte clone 2398682CD1

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```

<400> 16
Met Arg Gly Lys Thr Phe Arg Phe Glu Met Gln Arg Asp Leu Val
 1      5      10      15
Ser Phe Pro Leu Ser Pro Ala Val Arg Val Lys Leu Val Ser Ala
      20      25      30
Gly Phe Gln Thr Ala Glu Glu Leu Leu Glu Val Lys Pro Ser Glu
      35      40      45
Leu Ser Lys Glu Val Gly Ile Ser Lys Ala Glu Ala Leu Glu Thr
      50      55      60
Leu Gln Ile Ile Arg Arg Glu Cys Leu Thr Asn Lys Pro Arg Tyr
      65      70      75
Ala Gly Thr Ser Glu Ser His Lys Lys Cys Thr Ala Leu Glu Leu
      80      85      90
Leu Glu Gln Glu His Thr Gln Gly Phe Ile Ile Thr Phe Cys Ser
      95      100     105
Ala Leu Asp Asp Ile Leu Gly Gly Gly Val Pro Leu Met Lys Thr
      110     115     120
Thr Glu Ile Cys Gly Ala Pro Gly Val Gly Lys Thr Gln Leu Cys
      125     130     135
Met Gln Leu Ala Val Asp Val Gln Ile Pro Glu Cys Phe Gly Gly
      140     145     150
Val Ala Gly Glu Ala Val Phe Ile Asp Thr Glu Gly Ser Phe Met
      155     160     165
Val Asp Arg Val Val Asp Leu Ala Thr Ala Cys Ile Gln His Leu
      170     175     180
Gln Leu Ile Ala Glu Lys His Lys Gly Glu Glu His Arg Lys Ala
      185     190     195

```

```

Leu Glu Asp Phe Thr Leu Asp Asn Ile Leu Ser His Ile Tyr Tyr
200 205
Phe Arg Cys Arg Asp Tyr Thr Glu Leu Leu Ala Gln Val Tyr Leu
215 220 225
Leu Pro Asp Phe Leu Ser Glu His Ser Lys Val Arg Leu Val Ile
230 235 240
Val Asp Gly Ile Ala Phe Pro Phe Arg His Asp Leu Asp Asp Leu
245 250 255
Ser Leu Arg Thr Arg Leu Leu Asn Gly Leu Ala Gln Gln Met Ile
260 265 270
Ser Leu Ala Asn Asn His Arg Leu Ala Val Ile Leu Thr Asn Gln
275 280 285
Met Thr Thr Lys Ile Asp Arg Asn Gln Ala Leu Leu Val Pro Ala
290 295 300
Leu Gly Glu Ser Trp Gly His Ala Ala Thr Ile Arg Leu Ile Phe
305 310 315
His Trp Asp Arg Lys Gln Arg Leu Ala Thr Leu Tyr Lys Ser Pro
320 325 330
Ser Gln Lys Glu Cys Thr Val Leu Phe Gln Ile Lys Pro Gln Gly
335 340 345
Phe Arg Asp Thr Val Thr Ser Ala Cys Ser Leu Gln Thr Glu
350 355 360
Gly Ser Leu Ser Thr Arg Lys Arg Ser Arg Asp Pro Glu Glu Glu
365 370 375
Leu

```

```

<210> 17
<211> 204
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte clone 2518753CD1

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```

<400> 17
Met Ala Lys Val Gln Val Asn Asn Val Val Val Leu Asp Asn Pro
1 5 10 15
Ser Pro Phe Tyr Asn Pro Phe Gln Phe Glu Ile Thr Phe Glu Cys
20 25 30
Ile Glu Asp Leu Ser Glu Asp Leu Glu Trp Lys Ile Ile Tyr Val
35 40 45
Gly Ser Ala Glu Ser Glu Glu Tyr Asp Gln Val Leu Asp Ser Val
50 55 60
Leu Val Gly Pro Val Pro Ala Gly Arg His Met Phe Val Phe Gln
65 70 75
Ala Asp Ala Pro Asn Pro Gly Leu Ile Pro Asp Ala Asp Ala Val
80 85 90
Gly Val Thr Val Val Leu Ile Thr Cys Thr Tyr Arg Gly Gln Glu
95 100 105
Phe Ile Arg Val Gly Tyr Tyr Val Asn Asn Glu Tyr Thr Glu Thr
110 115 120
Glu Leu Arg Glu Asn Pro Pro Val Lys Pro Asp Phe Ser Lys Leu
125 130 135
Gln Arg Asn Ile Leu Ala Ser Asn Pro Arg Val Thr Arg Phe His
140 145 150
Ile Asn Trp Glu Asp Asn Thr Glu Lys Leu Glu Asp Ala Glu Ser
155 160 165
Ser Asn Pro Asn Leu Gln Ser Leu Leu Ser Thr Asp Ala Leu Pro
170 175 180
Ser Ala Ser Lys Gly Trp Ser Thr Ser Glu Asn Ser Leu Asn Val
185 190 195
Met Leu Glu Ser His Met Asp Cys Met

```

200

<210> 18
 <211> 713
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 2709055CD1

<400> 18
 Met Tyr Leu Leu Ile Gln Met Cys Tyr His Leu Ala Leu Pro Trp
 1 5 10 15
 Tyr Ser Lys Tyr Phe Pro Tyr Leu Ala Leu Ile His Thr Ile Ile
 20 25 30
 Leu Met Ala Ser Ser Asn Phe Trp Phe Lys Tyr Pro Lys Thr Cys
 35 40 45
 Ser Lys Val Glu His Ser Val Ser Ile Leu Gly Lys Cys Phe Glu
 50 55 60
 Ser Pro Trp Thr Thr Lys Ala Leu Ser Glu Thr Ala Cys Glu Asp
 65 70 75
 Ser Glu Glu Asn Lys Gln Arg Ile Thr Gly Ala Gln Thr Leu Pro
 80 85 90
 Lys His Val Ser Thr Ser Ser Asp Glu Gly Ser Pro Ser Ala Ser
 95 100 105
 Thr Pro Met Ile Asn Lys Thr Gly Phe Lys Phe Ser Ala Glu Lys
 110 115 120
 Pro Val Ile Glu Val Pro Ser Met Thr Ile Leu Asp Lys Lys Asp
 125 130 135
 Gly Glu Gln Ala Lys Ala Leu Phe Glu Lys Val Arg Lys Phe Arg
 140 145 150
 Ala His Val Glu Asp Ser Asp Leu Ile Tyr Lys Leu Tyr Val Val
 155 160 165
 Gln Thr Val Ile Lys Thr Ala Lys Phe Ile Phe Ile Leu Cys Tyr
 170 175 180
 Thr Ala Asn Phe Val Asn Ala Ile Ser Phe Glu His Val Cys Lys
 185 190 195
 Pro Lys Val Glu His Leu Ile Gly Tyr Glu Val Phe Glu Cys Thr
 200 205 210
 His Asn Met Ala Tyr Met Leu Lys Lys Leu Leu Ile Ser Tyr Ile
 215 220 225
 Ser Ile Ile Cys Val Tyr Gly Phe Ile Cys Leu Tyr Thr Leu Phe
 230 235 240
 Trp Leu Phe Arg Ile Pro Leu Lys Glu Tyr Ser Phe Glu Lys Val
 245 250 255
 Arg Glu Glu Ser Ser Phe Ser Asp Ile Pro Asp Val Lys Asn Asp
 260 265 270
 Phe Ala Phe Leu Leu His Met Val Asp Gln Tyr Asp Gln Leu Tyr
 275 280 285
 Ser Lys Arg Phe Gly Val Phe Leu Ser Glu Val Ser Glu Asn Lys
 290 295 300
 Leu Arg Glu Ile Ser Leu Asn His Glu Trp Thr Phe Glu Lys Leu
 305 310 315
 Arg Gln His Ile Ser Arg Asn Ala Gln Asp Lys Gln Glu Leu His
 320 325 330
 Leu Phe Met Leu Ser Gly Val Pro Asp Ala Val Phe Asp Leu Thr
 335 340 345
 Asp Leu Asp Val Leu Lys Leu Glu Leu Ile Pro Glu Ala Lys Ile
 350 355 360
 Pro Ala Lys Ile Ser Gln Met Thr Asn Leu Gln Glu Leu His Leu
 365 370 375
 Cys His Cys Pro Ala Lys Val Glu Gln Thr Ala Phe Ser Phe Leu

Arg Asp His Leu	380	Arg Cys Leu His Val	385	Lys Phe Thr Asp Val	390
	395		400		405
Glu Ile Pro Ala	410	Trp Val Tyr Leu Leu	415	Lys Asn Leu Arg Glu	420
Tyr Leu Ile Gly	425	Asn Leu Asn Ser Glu	430	Asn Asn Lys Met Ile	435
Leu Glu Ser Leu	440	Arg Glu Leu Arg His	445	Leu Lys Ile Leu His	450
Lys Ser Asn Leu	455	Thr Lys Val Pro Ser	460	Asn Ile Thr Asp Val	465
Pro His Leu Thr	470	Lys Leu Val Ile His	475	Asn Asp Gly Thr Lys	480
Leu Val Leu Asn	485	Ser Leu Lys Lys Met	490	Met Asn Val Ala Glu	495
Glu Leu Gln Asn	500	Cys Glu Leu Glu Arg	505	Ile Pro His Ala Ile	510
Ser Leu Ser Asn	515	Leu Gln Glu Leu Asp	520	Leu Lys Ser Asn Asn	525
Arg Thr Ile Glu	530	Glu Ile Ile Ser Phe	535	Gln His Leu Lys Arg	540
Thr Cys Leu Lys	545	Leu Trp His Asn Lys	550	Ile Val Thr Ile Pro	555
Ser Ile Thr His	560	Val Lys Asn Leu Glu	565	Ser Leu Tyr Phe Ser	570
Asn Lys Leu Glu	575	Ser Leu Pro Val Ala	580	Val Phe Ser Leu Gln	585
Leu Arg Cys Leu	590	Asp Val Ser Tyr Asn	595	Asn Ile Ser Met Ile	600
Ile Glu Ile Gly	605	Leu Leu Gln Asn Leu	610	Gln His Leu His Ile	615
Gly Asn Lys Val	620	Asp Ile Leu Pro Lys	625	Gln Leu Phe Lys Cys	630
Lys Leu Arg Thr	635	Leu Asn Leu Gly Gln	640	Asn Cys Ile Thr Ser	645
Pro Glu Lys Val	650	Gly Gln Leu Ser Gln	655	Leu Thr Gln Leu Glu	660
Lys Gly Asn Cys	665	Leu Asp Arg Leu Pro	670	Ala Gln Leu Gly Gln	675
Arg Met Leu Lys	680	Lys Ser Gly Leu Val	685	Val Glu Asp His Leu	690
Asp Thr Leu Pro	695	Leu Glu Val Lys Glu	700	Ala Leu Asn Gln Asp	705
Asn Ile Pro Phe	710	Ala Asn Gly Ile			

<210> 19
 <211> 360
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 2724537CD1

<400> 19
 Met Ala Ser Leu Leu Ala Lys Asp Ala Tyr Leu Gln Ser Leu Ala
 1 5 10 15
 Lys Lys Ile Cys Ser His Ser Ala Pro Glu Gln Gln Ala Arg Thr
 20 25 30
 Arg Ala Gly Lys Thr Gln Gly Ser Glu Thr Ala Gly Pro Pro Lys
 35 40 45
 Lys Lys Arg Lys Lys Thr Gln Lys Lys Phe Arg Lys Arg Glu Glu

	50		55		60									
Lys	Ala	Ala	Glu	His	Lys	Ala	Lys	Ser	Leu	Gly	Glu	Lys	Ser	Pro
	65		70		75									
Ala	Ala	Ser	Gly	Ala	Arg	Arg	Pro	Glu	Ala	Ala	Lys	Glu	Glu	Ala
	80		85		90									
Ala	Trp	Ala	Ser	Ser	Ser	Ala	Gly	Asn	Pro	Ala	Asp	Gly	Leu	Ala
	95		100		105									
Thr	Glu	Pro	Glu	Ser	Val	Phe	Ala	Leu	Asp	Val	Leu	Arg	Gln	Arg
	110		115		120									
Leu	His	Glu	Lys	Ile	Gln	Glu	Ala	Arg	Gly	Gln	Gly	Ser	Ala	Lys
	125		130		135									
Glu	Leu	Ser	Pro	Ala	Ala	Leu	Glu	Lys	Arg	Arg	Arg	Arg	Lys	Gln
	140		145		150									
Glu	Arg	Asp	Arg	Lys	Lys	Arg	Lys	Arg	Lys	Glu	Leu	Arg	Ala	Lys
	155		160		165									
Glu	Lys	Ala	Arg	Lys	Ala	Glu	Glu	Ala	Thr	Glu	Ala	Gln	Glu	Val
	170		175		180									
Val	Glu	Ala	Thr	Pro	Glu	Gly	Ala	Cys	Thr	Glu	Pro	Arg	Glu	Pro
	185		190		195									
Pro	Gly	Leu	Ile	Phe	Asn	Lys	Val	Glu	Val	Ser	Glu	Asp	Glu	Pro
	200		205		210									
Ala	Ser	Lys	Ala	Gln	Arg	Arg	Lys	Glu	Lys	Arg	Gln	Arg	Val	Lys
	215		220		225									
Gly	Asn	Leu	Thr	Pro	Leu	Thr	Gly	Arg	Asn	Tyr	Arg	Gln	Leu	Leu
	230		235		240									
Glu	Arg	Leu	Gln	Ala	Arg	Gln	Ser	Arg	Leu	Asp	Glu	Leu	Arg	Gly
	245		250		255									
Gln	Asp	Glu	Gly	Lys	Ala	Gln	Glu	Leu	Glu	Ala	Lys	Met	Lys	Trp
	260		265		270									
Thr	Asn	Leu	Leu	Tyr	Lys	Ala	Glu	Gly	Val	Lys	Ile	Arg	Asp	Asp
	275		280		285									
Glu	Arg	Leu	Leu	Gln	Glu	Ala	Leu	Lys	Arg	Lys	Glu	Lys	Arg	Arg
	290		295		300									
Ala	Gln	Arg	Gln	Arg	Arg	Trp	Glu	Lys	Arg	Thr	Ala	Gly	Val	Val
	305		310		315									
Glu	Lys	Met	Gln	Arg	Gln	Arg	Gln	Asp	Arg	Arg	Gln	Asn	Leu	Arg
	320		325		330									
Arg	Lys	Lys	Ala	Ala	Arg	Ala	Glu	Arg	Arg	Leu	Leu	Arg	Ala	Arg
	335		340		345									
Lys	Lys	Gly	Arg	Ile	Leu	Pro	Gln	Asp	Leu	Glu	Arg	Ala	Gly	Leu
	350		355		360									

<210> 20

<211> 196

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 025818CD1

<400> 20

Met	Pro	Ala	Asp	Ile	Met	Glu	Lys	Asn	Ser	Ser	Ser	Pro	Val	Ala
1				5					10					15
Ala	Thr	Pro	Ala	Ser	Val	Asn	Thr	Thr	Pro	Asp	Lys	Pro	Lys	Thr
				20					25					30
Ala	Ser	Glu	His	Arg	Lys	Ser	Ser	Lys	Pro	Ile	Met	Glu	Lys	Arg
				35					40					45
Arg	Arg	Ala	Arg	Ile	Asn	Glu	Ser	Leu	Ser	Gln	Leu	Lys	Thr	Leu
				50					55					60
Ile	Leu	Asp	Ala	Leu	Lys	Lys	Asp	Ser	Ser	Arg	His	Ser	Lys	Leu

		65						70					75	
Glu	Lys	Ala	Asp	Ile	Leu	Glu	Met	Thr	Val	Lys	His	Leu	Arg	Asn
		80								85				90
Leu	Gln	Arg	Ala	Gln	Met	Thr	Ala	Ala	Leu	Ser	Thr	Asp	Pro	Ser
		95								100				105
Val	Leu	Gly	Lys	Tyr	Arg	Ala	Gly	Phe	Ser	Glu	Cys	Met	Asn	Glu
		110								115				120
Val	Thr	Arg	Phe	Leu	Ser	Ser	Pro	Ser	Thr	Pro	Ala	Thr	Ala	Ala
		125								130				135
Pro	Pro	Trp	Ala	Pro	Thr	Gln	Cys	His	Leu	Pro	Ala	Ala	Pro	Arg
		140								145				150
Leu	Arg	Arg	Thr	Pro	Cys	Gly	Gly	Arg	Gly	Gly	Thr	Glu	Gly	Ala
		155								160				165
Gln	Ala	Thr	Pro	Pro	Pro	Lys	Leu	Pro	Asn	Pro	Pro	Leu	Phe	Pro
		170								175				180
Pro	Asp	Ser	Lys	Gln	Glu	Leu	Glu	Tyr	Trp	Glu	Arg	Arg	Gly	Leu
		185								190				195
Phe														

<210> 21
 <211> 540
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 438283CD1

<400> 21

Met	Leu	Arg	Glu	Glu	Ala	Thr	Lys	Lys	Ser	Lys	Glu	Lys	Glu	Pro
1				5					10					15
Gly	Met	Ala	Leu	Pro	Gln	Gly	Arg	Leu	Ala	Phe	Arg	Asp	Val	Ala
				20					25					30
Ile	Glu	Phe	Ser	Leu	Glu	Glu	Trp	Lys	Cys	Leu	Asn	Pro	Ala	Gln
				35					40					45
Arg	Ala	Leu	Tyr	Arg	Ala	Val	Met	Leu	Glu	Asn	Tyr	Arg	Asn	Leu
				50					55					60
Glu	Phe	Val	Asp	Ser	Ser	Leu	Lys	Ser	Met	Met	Glu	Phe	Ser	Ser
				65					70					75
Thr	Arg	His	Ser	Asn	Thr	Gly	Glu	Val	Ile	His	Thr	Gly	Thr	Leu
				80					85					90
Gln	Arg	His	Lys	Ser	His	His	Ile	Gly	Asp	Phe	Cys	Phe	Pro	Glu
				95					100					105
Met	Lys	Lys	Asp	Ile	His	His	Phe	Glu	Phe	Gln	Trp	Gln	Glu	Val
				110					115					120
Glu	Arg	Asn	Gly	His	Glu	Ala	Pro	Met	Thr	Lys	Ile	Lys	Lys	Leu
				125					130					135
Thr	Gly	Ser	Thr	Asp	Arg	Ser	Asp	His	Arg	His	Ala	Gly	Asn	Lys
				140					145					150
Pro	Ile	Lys	Asp	Gln	Leu	Gly	Leu	Ser	Phe	His	Ser	His	Leu	Pro
				155					160					165
Glu	Leu	His	Met	Phe	Gln	Thr	Lys	Gly	Lys	Ile	Ser	Asn	Gln	Leu
				170					175					180
Asp	Lys	Ser	Ile	Ser	Gly	Ala	Ser	Ser	Ala	Ser	Glu	Ser	Gln	Arg
				185					190					195
Ile	Ser	Cys	Arg	Leu	Lys	Thr	His	Ile	Ser	Asn	Lys	Tyr	Gly	Lys
				200					205					210
Asn	Phe	Leu	His	Ser	Ser	Phe	Thr	Gln	Ile	Gln	Glu	Ile	Cys	Met
				215					220					225
Arg	Glu	Lys	Pro	Cys	Gln	Ser	Asn	Glu	Cys	Gly	Lys	Ala	Phe	Asn
				230					235					240

Tyr Ser Ser Leu	Leu Arg Arg His His	Ile Thr His Ser Arg	Glu
245		250	255
Arg Glu Tyr Lys	Cys Asp Val Cys Gly	Lys Ile Phe Asn Gln	Lys
260		265	270
Gln Tyr Ile Val	Tyr His His Arg Cys	His Thr Gly Glu Lys	Thr
275		280	285
Tyr Lys Cys Asn	Glu Cys Gly Lys Thr	Phe Thr Gln Met Ser	Ser
290		295	300
Leu Val Cys His	Arg Arg Leu His Thr	Gly Glu Lys Pro Tyr	Lys
305		310	315
Cys Asn Glu Cys	Gly Lys Thr Phe Ser	Glu Lys Ser Ser Leu	Arg
320		325	330
Cys His Arg Arg	Leu His Thr Gly Glu	Lys Pro Tyr Lys Cys	Asn
335		340	345
Glu Cys Gly Lys	Thr Phe Gly Arg Asn	Ser Ala Leu Val Ile	His
350		355	360
Lys Ala Ile His	Thr Gly Glu Lys Pro	Tyr Lys Cys Asn Glu	Cys
365		370	375
Gly Lys Thr Phe	Ser Gln Lys Ser Ser	Leu Gln Cys His His	Ile
380		385	390
Leu His Thr Gly	Glu Lys Pro Tyr Lys	Cys Glu Glu Cys Asp	Asn
395		400	405
Val Tyr Ile Arg	Arg Ser His Leu Glu	Arg His Arg Lys Ile	His
410		415	420
Thr Gly Glu Gly	Ser Tyr Lys Cys Lys	Val Cys Asp Lys Ala	Phe
425		430	435
Arg Ser Asp Ser	Cys Leu Ala Asn His	Thr Arg Val His Thr	Gly
440		445	450
Glu Lys Pro Tyr	Lys Cys Asn Lys Cys	Ala Lys Val Phe Asn	Gln
455		460	465
Lys Gly Ile Leu	Ala Gln His Gln Arg	Val His Thr Gly Glu	Lys
470		475	480
Pro Tyr Lys Cys	Asn Glu Cys Gly Lys	Val Phe Asn Gln Lys	Ala
485		490	495
Ser Leu Ala Lys	His Gln Arg Val His	Thr Ala Glu Lys Pro	Tyr
500		505	510
Lys Cys Asn Glu	Cys Gly Lys Ala Phe	Thr Gly Gln Ser Thr	Leu
515		520	525
Ile His His Gln	Ala Ile His Gly Cys	Arg Glu Thr Leu Gln	Met
530		535	540

<210> 22

<211> 549

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 619699CD1

<400> 22

Met Leu Glu Asn Tyr	Lys Asn Leu Ala Thr	Val Gly Tyr Gln Leu
1	5	10
Phe Lys Pro Ser Leu	Ile Ser Trp Leu Glu	Gln Glu Glu Ser Arg
20		25
Thr Val Gln Arg Gly	Asp Phe Gln Ala Ser	Glu Trp Lys Val Gln
35		40
Leu Lys Thr Lys Glu	Leu Ala Leu Gln Gln	Asp Val Leu Gly Glu
50		55
Pro Thr Ser Ser Gly	Ile Gln Met Ile Gly	Ser His Asn Gly Gly
65		70
Glu Val Ser Asp Val	Lys Gln Cys Gly Asp	Val Ser Ser Glu His
80		85
		90

Ser	Cys	Leu	Lys	Thr	His	Val	Arg	Thr	Gln	Asn	Ser	Glu	Asn	Thr
				95					100					105
Phe	Glu	Cys	Tyr	Leu	Tyr	Gly	Val	Asp	Phe	Leu	Thr	Leu	His	Lys
				110					115					120
Lys	Thr	Ser	Thr	Gly	Glu	Gln	Arg	Ser	Val	Phe	Ser	Gln	Cys	Gly
				125					130					135
Lys	Ala	Phe	Ser	Leu	Asn	Pro	Asp	Val	Val	Cys	Gln	Arg	Thr	Cys
				140					145					150
Thr	Gly	Glu	Lys	Ala	Phe	Asp	Cys	Ser	Asp	Ser	Gly	Lys	Ser	Phe
				155					160					165
Ile	Asn	His	Ser	His	Leu	Gln	Gly	His	Leu	Arg	Thr	His	Asn	Gly
				170					175					180
Glu	Ser	Leu	His	Glu	Trp	Lys	Glu	Cys	Gly	Arg	Gly	Phe	Ile	His
				185					190					195
Ser	Thr	Asp	Leu	Ala	Val	Arg	Ile	Gln	Thr	His	Arg	Ser	Glu	Lys
				200					205					210
Pro	Tyr	Lys	Cys	Lys	Glu	Cys	Gly	Lys	Gly	Phe	Arg	Tyr	Ser	Ala
				215					220					225
Tyr	Leu	Asn	Ile	His	Met	Gly	Thr	His	Thr	Gly	Asp	Asn	Pro	Tyr
				230					235					240
Glu	Cys	Lys	Glu	Cys	Gly	Lys	Ala	Phe	Thr	Arg	Ser	Cys	Gln	Leu
				245					250					255
Thr	Gln	His	Arg	Lys	Thr	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	Cys
				260					265					270
Lys	Asp	Cys	Gly	Arg	Ala	Phe	Thr	Val	Ser	Ser	Cys	Leu	Ser	Gln
				275					280					285
His	Met	Lys	Ile	His	Val	Gly	Glu	Lys	Pro	Tyr	Glu	Cys	Lys	Glu
				290					295					300
Cys	Gly	Ile	Ala	Phe	Thr	Arg	Ser	Ser	Gln	Leu	Thr	Glu	His	Leu
				305					310					315
Lys	Thr	His	Thr	Ala	Lys	Asp	Pro	Phe	Glu	Cys	Lys	Val	Cys	Gly
				320					325					330
Lys	Ser	Phe	Arg	Asn	Ser	Ser	Cys	Leu	Ser	Asp	His	Phe	Arg	Ile
				335					340					345
His	Thr	Gly	Ile	Lys	Pro	Tyr	Lys	Cys	Lys	Asp	Cys	Gly	Lys	Ala
				350					355					360
Phe	Thr	Gln	Asn	Ser	Asp	Leu	Thr	Lys	His	Ala	Arg	Thr	His	Ser
				365					370					375
Gly	Glu	Arg	Pro	Tyr	Glu	Cys	Lys	Glu	Cys	Gly	Lys	Ala	Phe	Ala
				380					385					390
Arg	Ser	Ser	Arg	Leu	Ser	Glu	His	Thr	Arg	Thr	His	Thr	Gly	Glu
				395					400					405
Lys	Pro	Phe	Glu	Cys	Val	Lys	Cys	Gly	Lys	Ala	Phe	Ala	Ile	Ser
				410					415					420
Ser	Asn	Leu	Ser	Gly	His	Leu	Arg	Ile	His	Thr	Gly	Glu	Lys	Pro
				425					430					435
Phe	Glu	Cys	Leu	Glu	Cys	Gly	Lys	Ala	Phe	Thr	His	Ser	Ser	Ser
				440					445					450
Leu	Asn	Asn	His	Met	Arg	Thr	His	Ser	Ala	Lys	Lys	Pro	Phe	Thr
				455					460					465
Cys	Met	Glu	Cys	Gly	Lys	Ala	Phe	Lys	Phe	Pro	Thr	Cys	Val	Asn
				470					475					480
Leu	His	Met	Arg	Ile	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	Cys	Lys
				485					490					495
Gln	Cys	Gly	Lys	Ser	Phe	Ser	Tyr	Ser	Asn	Ser	Phe	Gln	Leu	His
				500					505					510
Glu	Arg	Thr	His	Thr	Gly	Glu	Lys	Pro	Tyr	Glu	Cys	Lys	Glu	Cys
				515					520					525
Gly	Lys	Ala	Phe	Ser	Ser	Ser	Ser	Ser	Phe	Arg	Asn	His	Glu	Arg
				530					535					540
Arg	His	Ala	Asp	Glu	Arg	Leu	Ser	Ala						
				545										

WO 99/57144

PCT/US99/09935

<210> 23
<211> 361
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte clone 693452CD1

<400> 23

Met	Ala	Asp	Phe	Lys	Val	Leu	Ser	Ser	Gln	Asp	Ile	Lys	Trp	Ala	
1				5					10					15	
Leu	His	Glu	Leu	Lys	Gly	His	Tyr	Ala	Ile	Thr	Arg	Lys	Ala	Leu	
				20					25					30	
Ser	Asp	Ala	Ile	Lys	Lys	Trp	Gln	Glu	Leu	Ser	Pro	Glu	Thr	Ser	
				35					40					45	
Gly	Lys	Arg	Lys	Lys	Arg	Lys	Gln	Met	Asn	Gln	Tyr	Ser	Tyr	Ile	
				50					55					60	
Asp	Phe	Lys	Phe	Glu	Gln	Gly	Asp	Ile	Lys	Ile	Glu	Lys	Arg	Met	
				65					70					75	
Phe	Phe	Leu	Glu	Asn	Lys	Arg	Arg	His	Cys	Arg	Ser	Tyr	Asp	Arg	
				80					85					90	
Arg	Ala	Leu	Leu	Pro	Ala	Val	Gln	Gln	Glu	Gln	Glu	Phe	Tyr	Glu	
				95					100					105	
Gln	Lys	Ile	Lys	Glu	Met	Ala	Glu	His	Glu	Asp	Phe	Leu	Leu	Ala	
				110					115					120	
Leu	Gln	Met	Asn	Glu	Glu	Gln	Tyr	Gln	Lys	Asp	Gly	Gln	Leu	Ile	
				125					130					135	
Glu	Cys	Arg	Cys	Cys	Tyr	Gly	Glu	Phe	Pro	Phe	Glu	Glu	Leu	Thr	
				140					145					150	
Gln	Cys	Ala	Asp	Ala	His	Leu	Phe	Cys	Lys	Glu	Cys	Leu	Ile	Arg	
				155					160					165	
Tyr	Ala	Gln	Glu	Ala	Val	Phe	Gly	Ser	Gly	Lys	Leu	Glu	Leu	Ser	
				170					175					180	
Cys	Met	Glu	Gly	Ser	Cys	Thr	Cys	Ser	Phe	Pro	Thr	Ser	Glu	Leu	
				185					190					195	
Glu	Lys	Val	Leu	Pro	Gln	Thr	Ile	Leu	Tyr	Lys	Tyr	Tyr	Glu	Arg	
				200					205					210	
Lys	Ala	Glu	Glu	Glu	Val	Ala	Ala	Ala	Tyr	Ala	Asp	Glu	Leu	Val	
				215					220					225	
Arg	Cys	Pro	Ser	Cys	Ser	Phe	Pro	Ala	Leu	Leu	Asp	Ser	Asp	Val	
				230					235					240	
Lys	Arg	Phe	Ser	Cys	Pro	Asn	Pro	His	Cys	Arg	Lys	Glu	Thr	Cys	
				245					250					255	
Arg	Lys	Cys	Gln	Gly	Leu	Trp	Lys	Glu	His	Asn	Gly	Leu	Thr	Cys	
				260					265					270	
Glu	Glu	Leu	Ala	Glu	Lys	Asp	Asp	Ile	Lys	Tyr	Arg	Thr	Ser	Ile	
				275					280					285	
Glu	Glu	Lys	Met	Thr	Ala	Ala	Arg	Ile	Arg	Lys	Cys	His	Lys	Cys	
				290					295					300	
Gly	Thr	Gly	Leu	Ile	Lys	Ser	Glu	Gly	Cys	Asn	Arg	Met	Ser	Cys	
				305					310					315	
Arg	Cys	Gly	Ala	Gln	Met	Cys	Tyr	Leu	Cys	Arg	Val	Ser	Ile	Asn	
				320					325					330	
Gly	Tyr	Asp	His	Xaa	Cys	Gln	Gln	Ser	Arg	Leu	Thr	Gly	Ala	Pro	
				335					340					345	
Phe	Gln	Gly	Val	Phe	Lys	Met	Leu	Ser	Met	Asp	Arg	Leu	Gln	Cys	
				350					355					360	
Lys															

<210> 24
 <211> 241
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 839651CD1

<400> 24
 Met Trp Pro Ser Leu Glu Ala Leu Cys Ser Leu Phe Ala Ala Arg
 1 5 10 15
 Ser Thr Gly Ser Gln Ala Gln Ser Ala Pro Thr Pro Ala Trp Asp
 20 25 30
 Glu Asp Thr Ala Gln Ile Gly Pro Lys Arg Ile Arg Lys Ala Ala
 35 40 45
 Lys Arg Glu Leu Met Pro Cys Asp Phe Pro Gly Cys Gly Arg Ile
 50 55 60
 Phe Ser Asn Arg Gln Tyr Leu Asn His His Lys Lys Tyr Gln His
 65 70 75
 Ile His Gln Lys Ser Phe Ser Cys Pro Glu Pro Ala Cys Gly Lys
 80 85 90
 Ser Phe Asn Phe Lys Lys His Leu Lys Glu His Met Lys Leu His
 95 100 105
 Ser Asp Thr Arg Asp Tyr Ile Cys Glu Phe Cys Ala Arg Ser Phe
 110 115 120
 Arg Thr Ser Ser Asn Leu Val Ile His Arg Arg Ile His Thr Gly
 125 130 135
 Glu Lys Pro Leu Gln Cys Glu Ile Cys Gly Phe Thr Cys Arg Gln
 140 145 150
 Lys Ala Ser Leu Asn Trp His Gln Arg Lys His Ala Glu Thr Val
 155 160 165
 Ala Ala Leu Arg Phe Pro Cys Glu Phe Cys Gly Lys Arg Phe Glu
 170 175 180
 Lys Pro Asp Ser Val Ala Ala His Arg Ser Lys Ser His Pro Ala
 185 190 195
 Leu Leu Leu Ala Pro Gln Glu Ser Pro Ser Gly Pro Leu Glu Pro
 200 205 210
 Cys Pro Ser Ile Ser Ala Pro Gly Pro Leu Gly Ser Ser Glu Gly
 215 220 225
 Ser Arg Pro Ser Ala Ser Pro Gln Ala Pro Thr Leu Leu Pro Gln
 230 235 240
 Gln

<210> 25
 <211> 576
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 1253545CD1

<400> 25
 Met Ala Lys Ala Gln Glu Thr Gly His Leu Val Met Asp Val Arg
 1 5 10 15
 Arg Tyr Gly Lys Ala Gly Ser Pro Glu Thr Lys Trp Ile Asp Ala
 20 25 30
 Thr Ser Gly Ile Tyr Asn Ser Glu Lys Ser Ser Asn Leu Ser Val
 35 40 45
 Thr Thr Asp Phe Ser Glu Ser Leu Gln Ser Ser Asn Ile Glu Ser

	50		55		60									
Lys	Glu	Ile	Asn	Gly	Ile	His	Asp	Glu	Ser	Asn	Ala	Phe	Glu	Ser
	65		70		75									
Lys	Ala	Ser	Glu	Ser	Ile	Ser	Leu	Lys	Asn	Leu	Lys	Arg	Arg	Ser
	80		85		90									
Gln	Phe	Phe	Glu	Gln	Gly	Ser	Ser	Asp	Ser	Val	Val	Pro	Asp	Leu
	95		100		105									
Pro	Val	Pro	Thr	Ile	Ser	Ala	Pro	Ser	Arg	Trp	Val	Trp	Asp	Gln
	110		115		120									
Glu	Glu	Glu	Arg	Lys	Arg	Gln	Glu	Arg	Trp	Gln	Lys	Glu	Gln	Asp
	125		130		135									
Arg	Leu	Leu	Gln	Glu	Lys	Tyr	Gln	Arg	Glu	Gln	Glu	Lys	Leu	Arg
	140		145		150									
Glu	Glu	Trp	Gln	Arg	Ala	Lys	Gln	Glu	Ala	Glu	Arg	Glu	Asn	Ser
	155		160		165									
Lys	Tyr	Leu	Asp	Glu	Glu	Leu	Met	Val	Leu	Ser	Ser	Asn	Ser	Met
	170		175		180									
Ser	Leu	Thr	Thr	Arg	Glu	Pro	Ser	Leu	Ala	Thr	Trp	Glu	Ala	Thr
	185		190		195									
Trp	Ser	Glu	Gly	Ser	Lys	Ser	Ser	Asp	Arg	Glu	Gly	Thr	Arg	Ala
	200		205		210									
Gly	Glu	Glu	Glu	Arg	Arg	Gln	Pro	Gln	Glu	Glu	Val	Val	His	Glu
	215		220		225									
Asp	Gln	Gly	Lys	Lys	Pro	Gln	Asp	Gln	Leu	Val	Ile	Glu	Arg	Glu
	230		235		240									
Arg	Lys	Trp	Glu	Gln	Gln	Leu	Gln	Glu	Glu	Gln	Glu	Gln	Lys	Arg
	245		250		255									
Leu	Gln	Ala	Glu	Ala	Glu	Glu	Gln	Lys	Arg	Pro	Ala	Glu	Glu	Gln
	260		265		270									
Lys	Arg	Gln	Ala	Glu	Ile	Glu	Arg	Glu	Thr	Ser	Val	Arg	Ile	Tyr
	275		280		285									
Gln	Tyr	Arg	Arg	Pro	Val	Asp	Ser	Tyr	Asp	Ile	Pro	Lys	Thr	Glu
	290		295		300									
Glu	Ala	Ser	Ser	Gly	Phe	Leu	Pro	Gly	Asp	Arg	Asn	Lys	Ser	Arg
	305		310		315									
Ser	Thr	Thr	Glu	Leu	Asp	Asp	Tyr	Ser	Thr	Asn	Lys	Asn	Gly	Asn
	320		325		330									
Asn	Lys	Tyr	Leu	Asp	Gln	Ile	Gly	Asn	Thr	Thr	Ser	Ser	Gln	Arg
	335		340		345									
Arg	Ser	Lys	Lys	Glu	Gln	Val	Pro	Ser	Gly	Ala	Glu	Leu	Glu	Arg
	350		355		360									
Gln	Gln	Ile	Leu	Gln	Glu	Met	Arg	Lys	Arg	Thr	Pro	Leu	His	Asn
	365		370		375									
Asp	Asn	Ser	Trp	Ile	Arg	Gln	Arg	Ser	Ala	Ser	Val	Asn	Lys	Glu
	380		385		390									
Pro	Val	Ser	Leu	Pro	Gly	Ile	Met	Arg	Arg	Gly	Glu	Ser	Leu	Asp
	395		400		405									
Asn	Leu	Asp	Ser	Pro	Arg	Ser	Asn	Ser	Trp	Arg	Gln	Pro	Pro	Trp
	410		415		420									
Leu	Asn	Gln	Pro	Thr	Gly	Phe	Tyr	Ala	Ser	Ser	Ser	Val	Gln	Asp
	425		430		435									
Phe	Ser	Arg	Pro	Gln	Pro	Gln	Leu	Val	Ser	Thr	Ser	Asn	Arg	Ala
	440		445		450									
Tyr	Met	Arg	Asn	Pro	Ser	Ser	Ser	Val	Pro	Pro	Pro	Ser	Ala	Gly
	455		460		465									
Ser	Val	Lys	Thr	Ser	Thr	Thr	Gly	Val	Ala	Thr	Thr	Gln	Ser	Pro
	470		475		480									
Thr	Pro	Arg	Ser	His	Ser	Pro	Ser	Ala	Ser	Gln	Ser	Gly	Ser	Gln
	485		490		495									
Leu	Arg	Asn	Arg	Ser	Val	Ser	Gly	Lys	Arg	Ile	Cys	Ser	Tyr	Cys
	500		505		510									
Asn	Asn	Ile	Leu	Gly	Lys	Gly	Ala	Ala	Met	Ile	Ile	Glu	Ser	Leu
	515		520		525									
Gly	Leu	Cys	Tyr	His	Leu	His	Cys	Phe	Lys	Cys	Val	Ala	Cys	Glu

	530		535		540
Cys Asp Leu Gly	Gly Ser Ser Ser Gly	Ala Glu Val Arg Ile	Arg		
	545		550		555
Asn His Gln Leu Tyr	Cys Asn Asp Cys Tyr	Leu Arg Phe Lys	Ser		
	560		565		570
Gly Arg Pro Thr Ala	Met				
	575				

<210> 26

<211> 408

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1425691CD1

<400> 26

Met Pro Gly His Leu Gln Glu Gly Phe Gly Cys Val Val Thr Asn	
1 5 10 15	
Arg Phe Asp Gln Leu Phe Asp Asp Glu Ser Asp Pro Phe Glu Val	
20 25 30	
Leu Lys Ala Ala Glu Asn Lys Lys Lys Glu Ala Gly Gly Gly Gly	
35 40 45	
Val Gly Gly Pro Gly Ala Lys Ser Ala Ala Gln Ala Ala Ala Gln	
50 55 60	
Thr Asn Ser Asn Ala Ala Gly Lys Gln Leu Arg Lys Glu Ser Gln	
65 70 75	
Lys Asp Arg Lys Asn Pro Leu Pro Pro Ser Val Gly Val Val Asp	
80 85 90	
Lys Lys Glu Glu Thr Gln Pro Pro Val Ala Leu Lys Lys Glu Gly	
95 100 105	
Ile Arg Arg Val Gly Arg Arg Pro Asp Gln Gln Leu Gln Gly Glu	
110 115 120	
Gly Lys Ile Ile Asp Arg Arg Pro Glu Arg Arg Pro Pro Arg Glu	
125 130 135	
Arg Arg Phe Glu Lys Pro Leu Glu Glu Lys Gly Glu Gly Gly Glu	
140 145 150	
Phe Ser Val Asp Arg Pro Ile Ile Asp Arg Pro Ile Arg Gly Arg	
155 160 165	
Gly Gly Leu Gly Arg Gly Arg Gly Gly Arg Gly Arg Gly Met Gly	
170 175 180	
Arg Gly Asp Gly Phe Asp Ser Arg Gly Lys Arg Glu Phe Asp Arg	
185 190 195	
His Ser Gly Ser Asp Arg Ser Ser Phe Ser His Tyr Ser Gly Leu	
200 205 210	
Lys His Glu Asp Lys Arg Gly Gly Ser Gly Ser His Asn Trp Gly	
215 220 225	
Thr Val Lys Asp Glu Leu Thr Glu Ser Pro Lys Tyr Ile Gln Lys	
230 235 240	
Gln Ile Ser Tyr Asn Tyr Ser Asp Leu Asp Gln Ser Asn Val Thr	
245 250 255	
Glu Glu Thr Pro Glu Gly Glu Glu His His Pro Val Ala Asp Thr	
260 265 270	
Glu Asn Lys Glu Asn Glu Val Glu Glu Val Lys Glu Glu Gly Pro	
275 280 285	
Lys Glu Met Thr Leu Asp Glu Trp Lys Ala Ile Gln Asn Lys Asp	
290 295 300	
Arg Ala Lys Val Glu Phe Asn Ile Arg Lys Pro Asn Glu Gly Ala	
305 310 315	
Asp Gly Gln Trp Lys Lys Gly Phe Val Leu His Lys Ser Lys Ser	
320 325 330	
Glu Glu Ala His Ala Glu Asp Ser Val Met Asp His His Phe Arg	

	335		340		345
Lys Pro Ala Asn Asp Ile Thr Ser Gln Leu Glu Ile Asn Phe Gly					
	350		355		360
Asp Leu Gly Arg Pro Gly Arg Gly Gly Arg Gly Gly Arg Gly Gly					
	365		370		375
Arg Gly Arg Gly Gly Arg Pro Asn Arg Gly Ser Arg Thr Asp Lys					
	380		385		390
Ser Ser Ala Ser Ala Pro Asp Val Asp Asp Pro Glu Ala Phe Pro					
	395		400		405
Ala Leu Ala					

<210> 27

<211> 810

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1484257CD1

<400> 27

Met Asp Phe Pro Gln His Ser Gln His Val Leu Glu Gln Leu Asn		
1 5 10 15		
Gln Gln Arg Gln Leu Gly Leu Leu Cys Asp Cys Thr Phe Val Val		
20 25 30		
Asp Gly Val His Phe Lys Ala His Lys Ala Val Leu Ala Ala Cys		
35 40 45		
Ser Glu Tyr Phe Lys Met Leu Phe Val Asp Gln Lys Asp Val Val		
50 55 60		
His Leu Asp Ile Ser Asn Ala Ala Gly Leu Gly Gln Val Leu Glu		
65 70 75		
Phe Met Tyr Thr Ala Lys Leu Ser Leu Ser Pro Glu Asn Val Asp		
80 85 90		
Asp Val Leu Ala Val Ala Thr Phe Leu Gln Met Gln Asp Ile Ile		
95 100 105		
Thr Ala Cys His Ala Leu Lys Ser Leu Ala Glu Pro Ala Thr Ser		
110 115 120		
Pro Gly Gly Asn Ala Glu Ala Leu Ala Gln Lys Val Cys Pro Val		
125 130 135		
Pro Ser Pro Gly Gly Asp Lys Arg Ala Lys Glu Glu Lys Val Ala		
140 145 150		
Thr Ser Thr Leu Ser Arg Leu Glu Gln Ala Gly Arg Ser Thr Pro		
155 160 165		
Ile Gly Pro Ser Arg Asp Leu Lys Glu Glu Arg Gly Gly Gln Ala		
170 175 180		
Gln Ser Ala Ala Ser Gly Ala Glu Gln Thr Glu Lys Ala Asp Ala		
185 190 195		
Pro Arg Glu Pro Pro Pro Val Glu Leu Lys Pro Asp Pro Thr Ser		
200 205 210		
Gly Met Ala Ala Ala Glu Ala Glu Ala Ala Leu Ser Glu Ser Ser		
215 220 225		
Glu Gln Glu Met Glu Val Glu Pro Ala Arg Lys Gly Glu Glu Glu		
230 235 240		
Gln Lys Glu Gln Glu Glu Gln Glu Glu Gly Ala Gly Pro Ala		
245 250 255		
Glu Val Lys Glu Glu Gly Ser Gln Leu Glu Asn Gly Glu Ala Pro		
260 265 270		
Glu Glu Asn Glu Asn Glu Glu Ser Ala Gly Thr Asp Ser Gly Gln		
275 280 285		
Glu Leu Gly Ser Glu Ala Arg Gly Leu Arg Ser Gly Thr Tyr Gly		
290 295 300		
Asp Arg Thr Glu Ser Lys Ala Tyr Gly Ser Val Ile His Lys Cys		
305 310 315		

Glu Asp Cys Gly	Lys	Glu Phe Thr His	Thr	Gly Asn Phe Lys	Arg
320			325		330
His Ile Arg Ile	His	Thr Gly Glu Lys	Pro	Phe Ser Cys Arg	Glu
335			340		345
Cys Ser Lys Ala	Phe	Ser Asp Pro Ala	Ala	Cys Glu Ala His	Glu
350			355		360
Lys Thr His Ser	Pro	Leu Lys Pro Tyr	Gly	Cys Glu Glu Cys	Gly
365			370		375
Lys Ser Tyr Arg	Leu	Ile Ser Leu Leu	Asn	Leu His Lys Lys	Arg
380			385		390
His Ser Gly Glu	Ala	Arg Tyr Arg Cys	Glu	Asp Cys Gly Lys	Leu
395			400		405
Phe Thr Thr Ser	Gly	Asn Leu Lys Arg	His	Gln Leu Val His	Ser
410			415		420
Gly Glu Lys Pro	Tyr	Gln Cys Asp Tyr	Cys	Gly Arg Ser Phe	Ser
425			430		435
Asp Pro Thr Ser	Lys	Met Arg His Leu	Glu	Thr His Asp Thr	Asp
440			445		450
Lys Glu His Lys	Cys	Pro His Cys Asp	Lys	Lys Phe Asn Gln	Val
455			460		465
Gly Asn Leu Lys	Ala	His Leu Lys Ile	His	Ile Ala Asp Gly	Pro
470			475		480
Leu Lys Cys Arg	Glu	Cys Gly Lys Gln	Phe	Thr Thr Ser Gly	Asn
485			490		495
Leu Lys Arg His	Leu	Arg Ile His Ser	Gly	Glu Lys Pro Tyr	Val
500			505		510
Cys Ile His Cys	Gln	Arg Gln Phe Ala	Asp	Pro Gly Ala Leu	Gln
515			520		525
Arg His Val Arg	Ile	His Thr Gly Glu	Lys	Pro Cys Gln Cys	Val
530			535		540
Met Cys Gly Lys	Ala	Phe Thr Gln Ala	Ser	Ser Leu Ile Ala	His
545			550		555
Val Arg Gln His	Thr	Gly Glu Lys Pro	Tyr	Val Cys Glu Arg	Cys
560			565		570
Gly Lys Arg Phe	Val	Gln Ser Ser Gln	Leu	Ala Asn His Ile	Arg
575			580		585
His His Asp Asn	Ile	Arg Pro His Lys	Cys	Ser Val Cys Ser	Lys
590			595		600
Ala Phe Val Asn	Val	Gly Asp Leu Ser	Lys	His Ile Ile Ile	His
605			610		615
Thr Gly Glu Lys	Pro	Tyr Leu Cys Asp	Lys	Cys Gly Arg Gly	Phe
620			625		630
Asn Arg Val Asp	Asn	Leu Arg Ser His	Val	Lys Thr Val His	Gln
635			640		645
Gly Lys Ala Gly	Ile	Lys Ile Leu Glu	Pro	Glu Glu Gly Ser	Glu
650			655		660
Val Ser Val Val	Thr	Val Asp Asp Met	Val	Thr Leu Ala Thr	Glu
665			670		675
Ala Leu Ala Ala	Thr	Ala Val Thr Gln	Leu	Thr Val Val Pro	Val
680			685		690
Gly Ala Ala Val	Thr	Ala Asp Glu Thr	Glu	Val Leu Lys Ala	Glu
695			700		705
Ile Ser Lys Ala	Val	Lys Gln Val Gln	Glu	Glu Asp Pro Asn	Thr
710			715		720
His Ile Leu Tyr	Ala	Cys Asp Ser Cys	Gly	Asp Lys Phe Leu	Asp
725			730		735
Ala Asn Ser Leu	Ala	Gln His Val Arg	Ile	His Thr Ala Gln	Ala
740			745		750
Leu Val Met Phe	Gln	Thr Asp Ala Asp	Phe	Tyr Gln Gln Tyr	Gly
755			760		765
Pro Gly Gly Thr	Trp	Pro Ala Gly Gln	Val	Leu Gln Ala Gly	Glu
770			775		780
Leu Val Phe Arg	Pro	Arg Asp Gly Ala	Glu	Gly Gln Pro Ala	Leu
785			790		795

Ala Glu Thr Ser Pro Thr Ala Pro Glu Cys Pro Pro Pro Ala Glu
800 805 810

<210> 28
<211> 324
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte clone 1732368CD1

<400> 28
Met Asp Trp Ser Glu Val Lys Glu Glu Lys Asp Asn Leu Glu Ile
1 5 10 15
Lys Gln Glu Glu Lys Phe Val Gly Gln Cys Ile Lys Glu Glu Leu
20 25 30
Met His Gly Glu Cys Val Lys Glu Glu Lys Asp Phe Leu Lys Lys
35 40 45
Glu Ile Val Asp Asp Thr Lys Val Lys Glu Glu Pro Pro Ile Asn
50 55 60
His Pro Val Gly Cys Lys Arg Lys Leu Ala Met Ser Arg Cys Glu
65 70 75
Thr Cys Gly Thr Glu Glu Ala Lys Tyr Arg Cys Pro Arg Cys Met
80 85 90
Arg Tyr Ser Cys Ser Leu Pro Cys Val Lys Lys His Lys Ala Glu
95 100 105
Leu Thr Cys Asn Gly Val Arg Asp Lys Thr Ala Tyr Ile Ser Ile
110 115 120
Gln Gln Phe Thr Glu Met Asn Leu Leu Ser Asp Tyr Arg Phe Leu
125 130 135
Glu Asp Val Ala Arg Thr Ala Asp His Ile Ser Arg Asp Ala Phe
140 145 150
Leu Lys Arg Pro Ile Ser Asn Lys Tyr Met Tyr Phe Met Lys Asn
155 160 165
Arg Ala Arg Arg Gln Gly Ile Asn Leu Lys Leu Leu Pro Asn Gly
170 175 180
Phe Thr Lys Arg Lys Glu Asn Ser Thr Phe Phe Asp Lys Lys Lys
185 190 195
Gln Gln Phe Cys Trp His Val Lys Leu Gln Phe Pro Gln Ser Gln
200 205 210
Ala Glu Tyr Ile Glu Lys Arg Val Pro Asp Asp Lys Thr Ile Asn
215 220 225
Glu Ile Leu Lys Pro Tyr Ile Asp Pro Glu Lys Ser Asp Pro Val
230 235 240
Ile Arg Gln Arg Leu Lys Ala Tyr Ile Arg Ser Gln Thr Gly Val
245 250 255
Gln Ile Leu Met Lys Ile Glu Tyr Met Gln Gln Asn Leu Val Arg
260 265 270
Tyr Tyr Glu Leu Asp Pro Tyr Lys Ser Leu Leu Asp Asn Leu Arg
275 280 285
Asn Lys Val Ile Ile Glu Tyr Pro Thr Leu His Val Val Leu Lys
290 295 300
Gly Ser Asn Asn Asp Met Lys Val Leu His Gln Val Lys Ser Glu
305 310 315
Ser Thr Lys Asn Val Gly Asn Glu Asn
320

<210> 29
<211> 292

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1870914CD1

<400> 29

```

Met Glu Glu Val Pro His Asp Cys Pro Gly Ala Asp Ser Ala Gln
 1          5          10          15
Ala Gly Arg Gly Ala Ser Cys Gln Gly Cys Pro Asn Gln Arg Leu
 20          25          30
Cys Ala Ser Gly Ala Gly Ala Thr Pro Asp Thr Ala Ile Glu Glu
 35          40          45
Ile Lys Glu Lys Met Lys Thr Val Lys His Lys Ile Leu Val Leu
 50          55          60
Ser Gly Lys Gly Gly Val Gly Lys Ser Thr Phe Ser Ala His Leu
 65          70          75
Ala His Gly Leu Ala Glu Asp Glu Asn Thr Gln Ile Ala Leu Leu
 80          85          90
Asp Ile Asp Ile Cys Gly Pro Ser Ile Pro Lys Ile Met Gly Leu
 95          100         105
Glu Gly Glu Gln Val His Gln Ser Gly Ser Gly Trp Ser Pro Val
 110         115         120
Tyr Val Glu Asp Asn Leu Gly Val Met Ser Val Gly Phe Leu Leu
 125         130         135
Ser Ser Pro Asp Asp Ala Val Ile Trp Arg Gly Pro Lys Lys Asn
 140         145         150
Gly Met Ile Lys Gln Phe Leu Arg Asp Val Asp Trp Gly Glu Val
 155         160         165
Asp Tyr Leu Ile Val Asp Thr Pro Pro Gly Thr Ser Asp Glu His
 170         175         180
Leu Ser Val Val Arg His Leu Ala Thr Ala His Ile Asp Gly Ala
 185         190         195
Val Ile Ile Thr Thr Pro Gln Glu Val Ser Leu Gln Asp Val Arg
 200         205         210
Lys Glu Ile Asn Phe Cys Arg Lys Val Lys Leu Pro Ile Ile Gly
 215         220         225
Val Val Glu Asn Met Ser Gly Phe Ile Cys Pro Lys Cys Lys Lys
 230         235         240
Glu Ser Gln Ile Phe Pro Pro Thr Thr Gly Gly Ala Glu Leu Met
 245         250         255
Cys Gln Asp Leu Glu Val Pro Leu Leu Gly Arg Val Pro Leu Asp
 260         265         270
Pro Leu Ile Gly Ile Gln Glu Phe Cys Asn Leu His Gln Ser Lys
 275         280         285
Glu Glu Asn Leu Ile Ser Ser
 290

```

<210> 30

<211> 259

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1910984CD1

<400> 30

```

Met Glu Cys His Leu Lys Thr His Tyr Lys Met Glu Tyr Lys Cys
 1          5          10          15
Arg Ile Cys Gln Thr Val Lys Ala Asn Gln Leu Glu Leu Glu Thr
 20          25          30

```

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His Thr Arg Glu His Arg Leu Gly Asn His Tyr Lys Cys Asp Gln
   35                               40                               45
Cys Gly Tyr Leu Ser Lys Thr Ala Asn Lys Leu Ile Glu His Val
   50                               55                               60
Arg Val His Thr Gly Glu Arg Pro Phe His Cys Asp Gln Cys Ser
   65                               70                               75
Tyr Ser Cys Thr Gly Lys Asp Asn Leu Asn Leu His Lys Lys Leu
   80                               85                               90
Lys His Ala Pro Arg Gln Thr Phe Ser Cys Glu Glu Cys Leu Phe
   95                               100                              105
Lys Thr Thr His Pro Phe Val Phe Ser Arg His Val Lys Lys His
  110                               115                              120
Gln Ser Gly Asp Cys Pro Glu Glu Asp Lys Lys Gly Leu Cys Pro
  125                               130                              135
Ala Pro Lys Glu Pro Ala Gly Pro Gly Ala Pro Leu Leu Val Val
  140                               145                              150
Gly Ser Ser Arg Asn Leu Leu Ser Pro Leu Ser Val Met Ser Ala
  155                               160                              165
Ser Gln Ala Leu Gln Thr Val Ala Leu Ser Ala Ala His Gly Ser
  170                               175                              180
Ser Ser Glu Pro Asn Leu Ala Leu Lys Ala Leu Ala Phe Asn Gly
  185                               190                              195
Ser Pro Leu Arg Phe Asp Lys Tyr Arg Asn Ser Asp Phe Ala His
  200                               205                              210
Leu Ile Pro Leu Thr Met Leu Tyr Pro Lys Asn His Leu Asp Leu
  215                               220                              225
Thr Phe His Pro Pro Arg Pro Gln Thr Ala Pro Pro Ser Ile Pro
  230                               235                              240
Ser Pro Lys His Ser Phe Leu Ala Tyr Leu Gly Leu Arg Glu Arg
  245                               250                              255
Ala Glu Thr Val

```

<210> 31
 <211> 97
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc feature
 <223> incyte clone 1943040CD1

```

<400> 31
Met Glu His His Ser Ser His Gly Gly Arg Lys Arg Tyr Ala Cys
   1                               5                               10                               15
Gln Gly Cys Trp Lys Thr Phe His Phe Ser Leu Ala Leu Ala Glu
   20                               25                               30
His Gln Lys Thr His Glu Lys Glu Lys Ser Tyr Ala Leu Gly Gly
   35                               40                               45
Ala Arg Gly Pro Gln Pro Ser Thr Arg Glu Pro Arg Arg Gly Leu
   50                               55                               60
Gly Arg Ala Val Pro Gln Arg Ala Trp Arg Ala Arg Leu Pro Pro
   65                               70                               75
His Pro Gln Arg Arg Arg Gly Glu Pro Leu Cys Cys Pro Val Pro
   80                               85                               90
Glu Gly Pro Leu Cys Arg Pro
   95

```

<210> 32
 <211> 812
 <212> PRT
 <213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2076520CD1

<400> 32

```

Met Ile Glu Pro Asp Gln Cys Phe Cys Arg Phe Asp Leu Thr Gly
 1           5           10           15
Thr Cys Asn Asp Asp Asp Cys Gln Trp Gln His Ile Gln Asp Tyr
           20           25           30
Thr Leu Ser Arg Lys Gln Leu Phe Gln Asp Ile Leu Ser Tyr Asn
           35           40           45
Leu Ser Leu Ile Gly Cys Ala Glu Thr Ser Thr Asn Glu Glu Ile
           50           55           60
Thr Ala Ser Ala Glu Lys Tyr Val Glu Lys Leu Phe Gly Val Asn
           65           70           75
Lys Asp Arg Met Ser Met Asp Gln Met Ala Val Leu Leu Val Ser
           80           85           90
Asn Ile Asn Glu Ser Lys Gly His Thr Pro Pro Phe Thr Thr Tyr
           95          100          105
Lys Asp Lys Arg Lys Trp Lys Pro Lys Phe Trp Arg Lys Pro Ile
          110          115          120
Ser Asp Asn Ser Phe Ser Ser Asp Glu Glu Gln Ser Thr Gly Pro
          125          130          135
Ile Lys Tyr Ala Phe Gln Pro Glu Asn Gln Ile Asn Val Pro Ala
          140          145          150
Leu Asp Thr Val Val Thr Pro Asp Asp Val Arg Tyr Phe Thr Asn
          155          160          165
Glu Thr Asp Asp Ile Ala Asn Leu Glu Ala Ser Val Leu Glu Asn
          170          175          180
Pro Ser His Val Gln Leu Trp Leu Lys Leu Ala Tyr Lys Tyr Leu
          185          190          195
Asn Gln Asn Glu Gly Glu Cys Ser Glu Ser Leu Asp Ser Ala Leu
          200          205          210
Asn Val Leu Ala Arg Ala Leu Glu Asn Asn Lys Asp Asn Pro Glu
          215          220          225
Ile Trp Cys His Tyr Leu Arg Leu Phe Ser Lys Arg Gly Thr Lys
          230          235          240
Asp Glu Val Gln Glu Met Cys Glu Thr Ala Val Glu Tyr Ala Pro
          245          250          255
Asp Tyr Gln Ser Phe Trp Thr Phe Leu His Leu Glu Ser Thr Phe
          260          265          270
Glu Glu Lys Asp Tyr Val Cys Glu Arg Met Leu Glu Phe Leu Met
          275          280          285
Gly Ala Ala Lys Gln Glu Thr Ser Asn Ile Leu Ser Phe Gln Leu
          290          295          300
Leu Glu Ala Leu Leu Phe Arg Val Gln Leu His Ile Phe Thr Gly
          305          310          315
Arg Cys Gln Ser Ala Leu Ala Ile Leu Gln Asn Ala Leu Lys Ser
          320          325          330
Ala Asn Asp Gly Ile Val Ala Glu Tyr Leu Lys Thr Ser Asp Arg
          335          340          345
Cys Leu Ala Trp Leu Ala Tyr Ile His Leu Ile Glu Phe Asn Ile
          350          355          360
Leu Pro Ser Lys Phe Tyr Asp Pro Ser Asn Asp Asn Pro Ser Arg
          365          370          375
Ile Val Asn Thr Glu Ser Phe Val Met Pro Trp Gln Ala Val Gln
          380          385          390
Asp Val Lys Thr Asn Pro Asp Met Leu Leu Ala Val Phe Glu Asp
          395          400          405
Ala Val Lys Ala Cys Thr Asp Glu Ser Leu Ala Val Glu Glu Arg
          410          415          420
Ile Glu Ala Cys Leu Pro Leu Tyr Thr Asn Met Ile Ala Leu His
          425          430          435
Gln Leu Leu Glu Arg Tyr Glu Ala Ala Met Glu Leu Cys Lys Ser

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Leu Leu Glu Ser Cys	Pro Ile Asn Cys	Gln Leu Leu Glu Ala Leu	440	445	450
455		460	465		
Val Ala Leu Tyr Leu	Gln Thr Asn Gln	His Asp Lys Ala Arg Ala	470	475	480
485		490	495		
Val Trp Leu Thr Ala	Phe Glu Lys Asn	Pro Gln Asn Ala Glu Val	500	505	510
515		520	525		
Asn Leu Leu Pro Phe	Leu Arg Lys Phe	Ile Ala Ser Phe Phe Lys	530	535	540
545		550	555		
Pro Gly Phe Glu Lys	Tyr Asn Asn Leu	Asp Leu Phe Arg Tyr Leu	560	565	570
575		580	585		
Gly Asn Phe Asp Asp	Met Phe Asn	His Gln Val Pro Tyr Leu	590	595	600
605		610	615		
Trp Leu Ile Tyr Cys	Leu Cys His Pro	Leu Gln Ser Ser Ile Lys	620	625	630
635		640	645		
Glu Thr Val Glu Ala	Tyr Glu Ala Ala	Leu Gly Val Ala Met Arg	650	655	660
665		670	675		
Cys Asp Ile Val Gln	Lys Ile Trp Met	Asp Tyr Leu Val Phe Ala	685	690	695
700		705	710		
Asn Asn Arg Ala Ala	Gly Ser Arg Asn	Lys Val Gln Glu Phe Arg	715	720	725
730		735	740		
Phe Phe Thr Asp Leu	Val Asn Arg Cys	Leu Val Thr Val Pro Ala	745	750	755
760		765	770		
Arg Tyr Pro Ile Pro	Phe Ser Ser Ala	Asp Tyr Trp Ser Asn Tyr	775	780	785
790		795	800		
Glu Phe His Asn Arg	Val Ile Phe Phe	Tyr Leu Ser Cys Val Pro	805	810	
815		820	825		
Lys Thr Gln His Ser	Lys Thr Leu Glu	Arg Phe Cys Ser Val Met	830	835	840
845		850	855		
Pro Ala Asn Ser Gly	Leu Ala Leu Arg	Leu Leu Gln His Glu Trp	860	865	870
875		880	885		
Glu Glu Ser Asn Val	Gln Ile Leu Lys	Leu Gln Ala Lys Met Phe	890	895	900
905		910	915		
Thr Tyr Asn Ile Pro	Thr Cys Leu Ala	Thr Trp Lys Ile Ala Ile	920	925	930
935		940	945		
Ala Ala Glu Ile Val	Leu Lys Gly Gln	Arg Glu Val His Arg Leu	950	955	960
965		970	975		
Tyr Gln Arg Ala Leu	Gln Lys Leu Pro	Leu Cys Ala Ser Leu Trp	980	985	990
995		1000	1005		
Lys Asp Gln Leu Leu	Phe Glu Ala Ser	Glu Gly Gly Lys Thr Asp	1010	1015	1020
1025		1030	1035		
Asn Leu Arg Lys Leu	Val Ser Lys Cys	Gln Glu Ile Gly Val Ser	1040	1045	1050
1055		1060	1065		
Leu Asn Glu Leu Leu	Asn Leu Asn Ser	Asn Lys Thr Glu Ser Lys	1070	1075	1080
1085		1090	1095		
Asn His					

<210> 33

<211> 392

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2291241CD1

<400> 33

Met Asp Ala Leu Val Glu Asp Asp Ile Cys Ile Leu Asn His Glu

1	5	10	15
Lys Ala His Lys Arg	Asp Thr Val Thr	Pro Val Ser Ile Tyr Ser	
20	25	30	
Gly Asp Glu Ser Val	Ala Ser His Phe Ala	Leu Val Thr Ala Tyr	
35	40	45	
Glu Asp Ile Lys Lys	Arg Leu Lys Asp Ser	Glu Lys Glu Asn Ser	
50	55	60	
Leu Leu Lys Lys Arg	Ile Arg Phe Leu Glu	Glu Lys Leu Ile Ala	
65	70	75	
Arg Phe Glu Glu Glu	Thr Ser Ser Val Gly	Arg Glu Gln Val Asn	
80	85	90	
Lys Ala Tyr His Ala	Tyr Arg Glu Val Cys	Ile Asp Arg Asp Asn	
95	100	105	
Leu Lys Ser Lys Leu	Asp Lys Met Asn Lys	Asp Asn Ser Glu Ser	
110	115	120	
Leu Lys Val Leu Asn	Glu Gln Leu Gln Ser	Lys Glu Val Glu Leu	
125	130	135	
Leu Gln Leu Arg Thr	Glu Val Glu Thr Gln	Gln Val Met Arg Asn	
140	145	150	
Leu Asn Pro Pro Ser	Asn Trp Glu Val Glu	Lys Leu Ser Cys	
155	160	165	
Asp Leu Lys Ile His	Gly Leu Glu Gln Glu	Leu Glu Leu Met Arg	
170	175	180	
Lys Glu Cys Ser Asp	Leu Lys Ile Glu Leu	Gln Lys Ala Lys Gln	
185	190	195	
Thr Asp Pro Tyr Gln	Glu Asp Asn Leu Lys	Ser Arg Asp Leu Gln	
200	205	210	
Lys Leu Ser Ile Ser	Ser Asp Asn Met Gln	His Ala Tyr Trp Glu	
215	220	225	
Leu Lys Arg Glu Met	Ser Asn Leu His Leu	Val Thr Gln Val Gln	
230	235	240	
Ala Glu Leu Leu Arg	Lys Leu Lys Thr Ser	Thr Ala Ile Lys Lys	
245	250	255	
Ala Cys Ala Pro Val	Gly Cys Ser Glu Asp	Leu Gly Arg Asp Ser	
260	265	270	
Thr Lys Leu His Leu	Met Asn Phe Thr Ala	Thr Tyr Thr Arg His	
275	280	285	
Pro Pro Leu Leu Pro	Asn Gly Lys Ala Leu	Cys His Thr Thr Ser	
290	295	300	
Ser Pro Leu Pro Gly	Asp Val Lys Val Leu	Ser Glu Lys Ala Ile	
305	310	315	
Leu Gln Ser Trp Thr	Asp Asn Glu Arg Ser	Ile Pro Asn Asp Gly	
320	325	330	
Thr Cys Phe Gln Glu	His Ser Ser Tyr Gly	Arg Asn Ser Leu Glu	
335	340	345	
Asp Asn Ser Trp Val	Phe Pro Ser Pro Pro	Lys Ser Ser Glu Thr	
350	355	360	
Ala Phe Gly Glu Thr	Lys Thr Lys Thr Leu	Pro Leu Pro Asn Leu	
365	370	375	
Pro Pro Leu His Tyr	Leu Asp Gln His Asn	Gln Asn Cys Leu Tyr	
380	385	390	
Lys Asn			

<210> 34

<211> 60

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> incyte clone 2329692CD1

<400> 34

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Met Ile Tyr Phe Phe Ile Ile Ile Val Glu Tyr Phe Tyr Gly Lys
 1           5           10           15
Ile Phe Val Val Leu Ile Ile Pro Ile Lys Ile Met Pro Asn Thr
           20           25           30
Lys Tyr Glu Phe Tyr Asp Val His Phe Val Leu Gly Ile Lys Arg
           35           40           45
Lys Lys His Thr Ser Trp Lys Ser Val Ser Cys Phe Leu Leu Leu
           50           55           60

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<210> 35

<211> 209

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2474110CD1

<400> 35

```

Met Asp Pro Ser Asp Ile Tyr Ala Val Ile Gln Ile Pro Gly Ser
 1           5           10           15
Arg Glu Phe Asp Val Ser Phe Arg Ser Ala Glu Lys Leu Ala Leu
           20           25           30
Phe Leu Arg Val Tyr Glu Glu Lys Arg Glu Gln Glu Asp Cys Trp
           35           40           45
Glu Asn Phe Val Val Leu Gly Arg Ser Lys Ser Ser Leu Lys Thr
           50           55           60
Leu Phe Ile Leu Phe Arg Asn Glu Thr Val Asp Val Glu Asp Ile
           65           70           75
Val Thr Trp Leu Lys Arg His Cys Asp Val Leu Ala Val Pro Val
           80           85           90
Lys Val Thr Asp Arg Phe Gly Ile Trp Thr Gly Glu Tyr Lys Cys
           95          100          105
Glu Ile Glu Leu Arg Gln Gly Glu Gly Gly Val Arg His Leu Pro
          110          115          120
Gly Ala Phe Phe Leu Gly Ala Glu Arg Gly Tyr Ser Trp Tyr Lys
          125          130          135
Gly Gln Pro Lys Thr Cys Phe Lys Cys Gly Ser Arg Thr His Met
          140          145          150
Ser Gly Ser Cys Thr Gln Asp Arg Cys Phe Arg Cys Arg Glu Glu
          155          160          165
Gly His Leu Ser Pro Tyr Cys Arg Lys Gly Ile Val Cys Asn Leu
          170          175          180
Cys Gly Lys Arg Gly His Ala Phe Ala Gln Cys Pro Lys Ala Val
          185          190          195
His Asn Ser Val Ala Ala Gln Leu Thr Gly Val Ala Gly His
          200          205

```

<210> 36

<211> 257

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2495790CD1

<400> 36

```

Met Val Gly Ala Gly Ile Ser Thr Pro Ser Gly Ile Pro Asp Phe
 1           5           10           15

```

```

Arg Ser Pro Gly Ser Gly Leu Tyr Ser Asn Leu Gln Gln Tyr Asp
      20                      25                      30
Leu Pro Tyr Pro Glu Ala Ile Phe Glu Leu Pro Phe Phe Phe His
      35                      40                      45
Asn Pro Lys Pro Phe Phe Thr Leu Ala Lys Glu Leu Tyr Pro Gly
      50                      55                      60
Asn Tyr Lys Pro Asn Val Thr His Tyr Phe Leu Arg Leu Leu His
      65                      70                      75
Asp Lys Gly Leu Leu Leu Arg Leu Tyr Thr Gln Asn Ile Asp Gly
      80                      85                      90
Leu Glu Arg Val Ser Gly Ile Pro Ala Ser Lys Leu Val Glu Ala
      95                      100                     105
His Gly Thr Phe Ala Ser Ala Thr Cys Thr Val Cys Gln Arg Pro
      110                     115                     120
Phe Pro Gly Glu Asp Ile Arg Ala Asp Val Met Ala Asp Arg Val
      125                     130                     135
Pro Arg Cys Pro Val Cys Thr Gly Val Val Lys Pro Asp Ile Val
      140                     145                     150
Phe Phe Gly Glu Pro Leu Pro Gln Arg Phe Leu Leu His Val Val
      155                     160                     165
Asp Phe Pro Met Ala Asp Leu Leu Leu Ile Leu Gly Thr Ser Leu
      170                     175                     180
Glu Val Glu Pro Phe Ala Ser Leu Thr Glu Ala Val Arg Ser Ser
      185                     190                     195
Val Pro Arg Leu Leu Ile Asn Arg Asp Leu Val Gly Pro Leu Ala
      200                     205                     210
Trp His Pro Arg Ser Arg Asp Val Ala Gln Leu Gly Asp Val Val
      215                     220                     225
His Gly Val Glu Ser Leu Val Glu Leu Leu Gly Trp Thr Glu Glu
      230                     235                     240
Met Arg Asp Leu Val Gln Arg Glu Thr Gly Lys Leu Asp Gly Pro
      245                     250                     255
Asp Lys

```

<210> 37

<211> 138

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2661254CD1

<400> 37

```

Met Ala Thr Lys Arg Leu Phe Gly Ala Thr Arg Thr Trp Ala Gly
      1      5      10
Trp Gly Ala Trp Glu Leu Leu Asn Pro Ala Thr Ser Gly Arg Leu
      20      25      30
Leu Ala Arg Asp Tyr Ala Lys Lys Pro Val Met Lys Gly Ala Lys
      35      40      45
Ser Gly Lys Gly Ala Val Thr Ser Glu Ala Leu Lys Asp Pro Asp
      50      55      60
Val Cys Thr Asp Pro Val Gln Leu Thr Thr Tyr Ala Met Gly Val
      65      70      75
Asn Ile Tyr Lys Glu Gly Gln Asp Val Pro Leu Lys Pro Asp Ala
      80      85      90
Glu Tyr Pro Glu Trp Leu Phe Glu Met Asn Leu Gly Pro Pro Lys
      95      100     105
Thr Leu Glu Glu Leu Asp Pro Glu Ser Arg Glu Tyr Trp Arg Arg
      110     115     120
Leu Arg Lys Gln Asn Ile Trp Arg His Asn Arg Leu Ser Lys Asn
      125     130     135

```

Lys Arg Leu

<210> 38

<211> 999

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2674047CD1

<400> 38

Met	Gly	Pro	Ser	Arg	Leu	Arg	Leu	Gly	Phe	Phe	Xaa	Lys	Arg	Gly
1				5					10					15
Cys	Ser	Arg	Ala	Met	Val	Glu	Ile	Glu	Leu	Phe	Arg	Ala	Ser	Gly
				20					25					30
Asn	Leu	Val	Ile	Thr	Arg	Glu	Ile	Asp	Val	Ala	Lys	Asn	Gln	Ser
				35					40					45
Phe	Trp	Phe	Ile	Asn	Lys	Lys	Ser	Thr	Thr	Gln	Xaa	Ile	Val	Glu
				50					55					60
Glu	Lys	Val	Ala	Ala	Leu	Asn	Ile	Gln	Val	Gly	Asn	Leu	Cys	Gln
				65					70					75
Phe	Leu	Pro	Gln	Asp	Lys	Val	Gly	Glu	Phe	Ala	Lys	Leu	Ser	Lys
				80					85					90
Ile	Glu	Leu	Leu	Glu	Ala	Thr	Glu	Lys	Ser	Ile	Gly	Pro	Pro	Glu
				95					100					105
Met	His	Lys	Tyr	His	Cys	Glu	Leu	Lys	Asn	Leu	Arg	Glu	Lys	Glu
				110					115					120
Lys	Gln	Leu	Glu	Thr	Ser	Cys	Lys	Glu	Lys	Thr	Glu	Tyr	Leu	Gln
				125					130					135
Lys	Met	Val	Gln	Arg	Asn	Glu	Arg	Tyr	Lys	Gln	Asp	Val	Glu	Arg
				140					145					150
Phe	Tyr	Glu	Arg	Lys	Arg	His	Leu	Asp	Leu	Ile	Glu	Met	Leu	Glu
				155					160					165
Ala	Lys	Arg	Pro	Trp	Val	Glu	Tyr	Glu	Asn	Val	Arg	Gln	Glu	Tyr
				170					175					180
Glu	Glu	Val	Lys	Leu	Val	Arg	Asp	Arg	Val	Lys	Glu	Glu	Val	Arg
				185					190					195
Lys	Leu	Lys	Glu	Gly	Gln	Ile	Pro	Ile	Thr	Cys	Arg	Ile	Glu	Glu
				200					205					210
Met	Glu	Asn	Glu	Arg	His	Asn	Leu	Glu	Ala	Arg	Ile	Lys	Glu	Lys
				215					220					225
Ala	Thr	Asp	Ile	Lys	Glu	Ala	Ser	Gln	Lys	Cys	Lys	Gln	Lys	Gln
				230					235					240
Asp	Val	Ile	Glu	Arg	Lys	Asp	Lys	His	Ile	Glu	Glu	Leu	Gln	Gln
				245					250					255
Ala	Leu	Ile	Val	Lys	Gln	Asn	Glu	Glu	Leu	Asp	Arg	Gln	Arg	Arg
				260					265					270
Ile	Gly	Asn	Thr	Arg	Lys	Met	Ile	Glu	Asp	Leu	Gln	Asn	Glu	Leu
				275					280					285
Lys	Thr	Thr	Glu	Asn	Cys	Glu	Asn	Leu	Gln	Pro	Gln	Ile	Asp	Ala
				290					295					300
Ile	Thr	Asn	Asp	Leu	Arg	Arg	Ile	Gln	Asp	Glu	Lys	Ala	Leu	Cys
				305					310					315
Glu	Gly	Glu	Ile	Ile	Asp	Lys	Arg	Arg	Glu	Arg	Glu	Thr	Leu	Glu
				320					325					330
Lys	Glu	Lys	Lys	Ser	Val	Asp	Asp	His	Ile	Val	Arg	Phe	Asp	Asn
				335					340					345
Leu	Met	Asn	Gln	Lys	Glu	Asp	Lys	Leu	Arg	Gln	Arg	Phe	Arg	Asp
				350					355					360
Thr	Tyr	Asp	Ala	Val	Leu	Trp	Leu	Arg	Asn	Asn	Arg	Asp	Lys	Phe
				365					370					375

Lys	Gln	Arg	Val	Cys	Glu	Pro	Ile	Met	Leu	Thr	Ile	Asn	Met	Lys
				380						385				390
Asp	Asn	Lys	Asn	Ala	Lys	Tyr	Ile	Glu	Asn	His	Ile	Pro	Ser	Asn
				395						400				405
Asp	Leu	Arg	Ala	Phe	Val	Phe	Glu	Ser	Gln	Glu	Asp	Met	Glu	Val
				410						415				420
Phe	Leu	Lys	Glu	Val	Arg	Asp	Asn	Lys	Lys	Leu	Arg	Val	Asn	Ala
				425						430				435
Val	Ile	Ala	Pro	Lys	Ser	Ser	Tyr	Ala	Asp	Lys	Ala	Pro	Ser	Arg
				440						445				450
Ser	Leu	Asn	Glu	Leu	Lys	Gln	Tyr	Gly	Phe	Phe	Ser	Tyr	Leu	Arg
				455						460				465
Glu	Leu	Phe	Asp	Ala	Pro	Asp	Pro	Val	Met	Ser	Tyr	Leu	Cys	Cys
				470						475				480
Gln	Tyr	His	Ile	His	Glu	Val	Pro	Val	Gly	Thr	Glu	Lys	Thr	Arg
				485						490				495
Glu	Arg	Ile	Glu	Arg	Val	Ile	Gln	Glu	Thr	Arg	Leu	Lys	Gln	Ile
				500						505				510
Tyr	Thr	Ala	Glu	Glu	Lys	Tyr	Val	Val	Lys	Thr	Ser	Phe	Tyr	Ser
				515						520				525
Asn	Lys	Val	Ile	Ser	Ser	Asn	Thr	Ser	Leu	Lys	Val	Ala	Gln	Phe
				530						535				540
Leu	Thr	Val	Thr	Val	Asp	Leu	Glu	Gln	Arg	Arg	His	Leu	Glu	Glu
				545						550				555
Gln	Leu	Lys	Glu	Ile	His	Arg	Lys	Leu	Gln	Ala	Val	Asp	Ser	Gly
				560						565				570
Leu	Ile	Ala	Leu	Arg	Glu	Thr	Ser	Lys	His	Leu	Glu	His	Lys	Asp
				575						580				585
Asn	Glu	Leu	Arg	Gln	Lys	Lys	Lys	Glu	Leu	Leu	Glu	Arg	Lys	Thr
				590						595				600
Lys	Lys	Arg	Gln	Leu	Glu	Gln	Lys	Ile	Ser	Ser	Lys	Leu	Gly	Ser
				605						610				615
Leu	Lys	Leu	Met	Glu	Gln	Asp	Thr	Cys	Asn	Leu	Glu	Glu	Glu	Glu
				620						625				630
Arg	Lys	Ala	Ser	Thr	Lys	Ile	Lys	Glu	Ile	Asn	Val	Gln	Lys	Ala
				635						640				645
Lys	Leu	Val	Thr	Glu	Leu	Thr	Asn	Leu	Ile	Lys	Ile	Cys	Thr	Ser
				650						655				660
Leu	His	Ile	Gln	Lys	Val	Asp	Leu	Ile	Leu	Gln	Asn	Thr	Thr	Val
				665						670				675
Ile	Ser	Glu	Lys	Asn	Lys	Leu	Glu	Ser	Asp	Tyr	Met	Ala	Ala	Ser
				680						685				690
Ser	Gln	Leu	Arg	Leu	Thr	Glu	Gln	His	Phe	Ile	Glu	Leu	Asp	Glu
				695						700				705
Asn	Arg	Gln	Arg	Leu	Leu	Gln	Lys	Cys	Lys	Glu	Leu	Met	Lys	Arg
				710						715				720
Ala	Arg	Gln	Val	Cys	Asn	Leu	Gly	Ala	Glu	Gln	Thr	Leu	Pro	Gln
				725						730				735
Glu	Tyr	Gln	Thr	Gln	Val	Pro	Thr	Ile	Pro	Asn	Gly	His	Asn	Ser
				740						745				750
Ser	Leu	Pro	Met	Val	Phe	Gln	Asp	Leu	Pro	Asn	Thr	Leu	Asp	Glu
				755						760				765
Ile	Asp	Ala	Leu	Leu	Thr	Glu	Glu	Arg	Ser	Arg	Ala	Ser	Cys	Phe
				770						775				780
Thr	Gly	Leu	Asn	Pro	Thr	Ile	Val	Gln	Glu	Tyr	Thr	Lys	Arg	Glu
				785						790				795
Glu	Glu	Ile	Glu	Gln	Leu	Thr	Glu	Glu	Leu	Lys	Gly	Lys	Lys	Val
				800						805				810
Glu	Leu	Asp	Gln	Tyr	Arg	Glu	Asn	Ile	Ser	Gln	Val	Lys	Glu	Arg
				815						820				825
Trp	Leu	Asn	Pro	Leu	Lys	Glu	Leu	Val	Glu	Lys	Ile	Asn	Glu	Lys
				830						835				840
Phe	Ser	Asn	Phe	Phe	Ser	Ser	Met	Gln	Cys	Ala	Gly	Glu	Val	Asp
				845						850				855

```

Leu His Thr Glu Asn Glu Glu Asp Tyr Asp Lys Tyr Gly Ile Arg
      860      865      870
Ile Arg Val Lys Phe Arg Ser Ser Thr Gln Leu His Glu Leu Thr
      875      880      885
Pro His His Gln Ser Gly Gly Glu Arg Ser Val Ser Thr Met Leu
      890      895      900
Tyr Leu Met Ala Leu Gln Glu Leu Asn Arg Cys Pro Phe Arg Val
      905      910      915
Val Asp Glu Ile Asn Gln Gly Met Asp Pro Ile Asn Glu Arg Arg
      920      925      930
Val Phe Glu Met Val Val Asn Thr Ala Cys Lys Glu Asn Thr Ser
      935      940      945
Gln Tyr Phe Phe Ile Thr Pro Lys Leu Leu Gln Asn Leu Pro Tyr
      950      955      960
Ser Glu Lys Met Thr Val Leu Phe Val Tyr Asn Gly Pro His Met
      965      970      975
Leu Glu Pro Asn Thr Trp Asn Leu Lys Ala Phe Gln Arg Arg Arg
      980      985      990
Arg Arg Ile Thr Phe Thr Gln Pro Ser
      995

```

<210> 39

<211> 377

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2762174CD1

<400> 39

```

Met Ala Glu Leu Glu Ser His Pro Cys Asp Ile Cys Gly Pro Ile
  1      5      10      15
Leu Lys Asp Thr Leu His Leu Ala Lys Tyr His Gly Gly Lys Ala
      20      25      30
Arg Gln Lys Pro Tyr Leu Cys Gly Ala Cys Gly Lys Gln Phe Trp
      35      40      45
Phe Ser Thr Asp Phe Asp Gln His Gln Asn Gln Pro Asn Gly Gly
      50      55      60
Lys Leu Phe Pro Arg Lys Glu Gly Arg Asp Ser Val Lys Ser Cys
      65      70      75
Arg Val His Val Pro Glu Lys Thr Leu Thr Cys Gly Lys Gly Arg
      80      85      90
Arg Asp Phe Ser Ala Thr Ser Gly Leu Leu Gln His Gln Ala Ser
      95      100      105
Leu Ser Ser Met Lys Pro His Lys Ser Thr Lys Leu Val Ser Gly
      110      115      120
Phe Leu Met Gly Gln Arg Tyr His Arg Cys Gly Glu Cys Gly Lys
      125      130      135
Ala Phe Thr Arg Lys Asp Thr Leu Ala Arg His Gln Arg Ile His
      140      145      150
Thr Gly Glu Arg Pro Tyr Glu Cys Asn Glu Cys Gly Lys Phe Phe
      155      160      165
Ser Gln Ser Tyr Asp Leu Phe Lys His Gln Thr Val His Thr Gly
      170      175      180
Glu Arg Pro Tyr Glu Cys Ser Glu Cys Gly Lys Phe Phe Arg Gln
      185      190      195
Ile Ser Gly Leu Ile Glu His Arg Arg Val His Thr Gly Glu Arg
      200      205      210
Leu Tyr Gln Cys Gly Lys Cys Gly Lys Phe Phe Ser Ser Lys Ser
      215      220      225
Asn Leu Ile Arg His Gln Glu Val His Thr Gly Ala Arg Pro Tyr
      230      235      240

```

```

Val Cys Ser Glu Cys Gly Lys Glu Phe Ser Arg Lys His Thr Leu
      245      250      255
Val Leu His Gln Arg Thr His Thr Gly Glu Arg Pro Tyr Glu Cys
      260      265      270
Ser Glu Cys Gly Lys Ala Phe Ser Gln Ser Ser His Leu Asn Val
      275      280      285
His Trp Arg Ile His Ser Ser Asp Tyr Glu Cys Ser Arg Cys Gly
      290      295      300
Lys Ala Phe Ser Cys Ile Ser Lys Leu Ile Gln His Gln Lys Val
      305      310      315
His Ser Gly Glu Lys Pro Tyr Glu Cys Ser Lys Cys Gly Lys Ala
      320      325      330
Phe Thr Gln Arg Pro Asn Leu Ile Arg His Trp Lys Val His Thr
      335      340      345
Gly Glu Arg Pro Tyr Val Cys Ser Glu Cys Gly Arg Glu Phe Ile
      350      355      360
Arg Lys Gln Thr Leu Val Leu His Gln Arg Val His Ala Gly Glu
      365      370      375
Lys Leu

```

```

<210> 40
<211> 324
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte clone 2765991CD1

```

```

<400> 40
Met Asp Phe Pro Lys His Asn Gln Ile Ile Thr Glu Glu Thr Gly
  1      5      10      15
Ser Ala Val Glu Pro Ser Asp Glu Ile Lys Arg Ala Ser Gly Asp
      20      25      30
Val Gln Thr Met Lys Ile Ser Ser Val Pro Asn Ser Leu Ser Lys
      35      40      45
Arg Asn Val Ser Leu Thr Arg Ser His Ser Val Gly Gly Pro Leu
      50      55      60
Gln Asn Ile Asp Phe Thr Gln Arg Pro Phe His Gly Ile Ser Thr
      65      70      75
Val Ser Leu Pro Gly Ser Leu Gln Glu Val Val Asp Pro Leu Gly
      80      85      90
Lys Arg Pro Asn Pro Pro Pro Val Ser Val Pro Tyr Leu Ser Pro
      95      100      105
Leu Val Leu Arg Lys Glu Leu Glu Ser Leu Leu Glu Asn Glu Gly
      110      115      120
Asp Gln Val Ile His Thr Ser Ser Phe Ile Asn Gln His Pro Ile
      125      130      135
Ile Phe Trp Asn Leu Val Trp Tyr Phe Arg Arg Leu Asp Leu Pro
      140      145      150
Ser Asn Leu Pro Gly Leu Ile Leu Thr Ser Glu His Cys Asn Glu
      155      160      165
Gly Val Gln Leu Pro Leu Ser Ser Leu Ser Gln Asp Ser Lys Leu
      170      175      180
Val Tyr Ile Arg Leu Leu Trp Asp Asn Ile Asn Leu His Gln Glu
      185      190      195
Pro Arg Glu Pro Leu Tyr Val Ser Trp Arg Asn Phe Asn Ser Glu
      200      205      210
Lys Lys Ser Ser Leu Leu Ser Glu Glu Gln Gln Glu Thr Ser Thr
      215      220      225
Leu Val Glu Thr Ile Arg Gln Ser Ile Gln His Asn Asn Val Leu
      230      235      240

```

```

Lys Pro Ile Asn Leu Leu Ser Gln Gln Met Lys Pro Gly Met Lys
245 250 255
Arg Gln Arg Ser Leu Tyr Arg Glu Ile Leu Phe Leu Ser Leu Val
260 265 270
Ser Leu Gly Arg Glu Asn Ile Asp Ile Glu Ala Phe Asp Asn Glu
275 280 285
Tyr Gly Ile Ala Tyr Asn Ser Leu Ser Ser Glu Ile Leu Glu Arg
290 295 300
Leu Gln Lys Ile Asp Ala Pro Pro Ser Ala Ser Val Glu Trp Cys
305 310 315
Arg Lys Cys Phe Gly Ala Pro Leu Ile
320

```

```

<210> 41
<211> 270
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> incyte clone 2775157CD1

```

```

<400> 41
Met Pro Cys Pro Met Leu Leu Pro Ser Gly Lys Val Ile Asp Gln
1 5 10 15
Ser Thr Leu Glu Lys Cys Asn Arg Ser Glu Ala Thr Trp Gly Arg
20 25 30
Val Pro Ser Asp Pro Phe Thr Gly Val Ala Phe Thr Pro His Ser
35 40 45
Gln Pro Leu Pro His Pro Ser Leu Lys Ala Arg Ile Asp His Phe
50 55 60
Leu Leu Gln His Ser Ile Pro Gly Cys His Leu Leu Gly Arg Ala
65 70 75
Gln Thr Ala Leu Ala Val Ile Pro Ser Ser Ile Val Leu Pro Ser
80 85 90
Gln Lys Arg Lys Ile Glu Gln Ala Glu His Val Pro Asp Ser Asn
95 100 105
Phe Gly Val Asn Ala Ser Cys Phe Ser Ala Thr Ser Pro Leu Val
110 115 120
Leu Pro Thr Thr Ser Glu His Thr Ala Lys Lys Met Lys Ala Thr
125 130 135
Asn Glu Pro Ser Leu Thr His Met Asp Cys Ser Thr Gly Pro Leu
140 145 150
Ser His Glu Gln Lys Leu Ser Gln Ser Leu Glu Ile Ala Leu Ala
155 160 165
Ser Thr Leu Gly Ser Met Pro Ser Phe Thr Ala Arg Leu Thr Arg
170 175 180
Gly Gln Leu Gln His Leu Gly Thr Arg Gly Ser Asn Thr Ser Trp
185 190 195
Arg Pro Gly Thr Gly Ser Glu Gln Pro Gly Ser Ile Leu Gly Pro
200 205 210
Glu Cys Ala Ser Cys Lys Arg Val Phe Ser Pro Tyr Phe Lys Lys
215 220 225
Glu Pro Val Tyr Gln Leu Pro Cys Gly His Leu Leu Cys Arg Pro
230 235 240
Cys Leu Gly Glu Lys Gln Arg Ser Leu Pro Met Thr Cys Thr Ala
245 250 255
Cys Gln Arg Pro Val Ala Ser Gln Asp Val Leu Arg Val His Phe
260 265 270

```

```

<210> 42
<211> 252

```

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2918375CD1

<400> 42

```

Met Leu Arg Lys Gly Ile Cys Glu Tyr His Glu Lys Asn Tyr Ala
 1          5          10          15
Ala Ala Leu Glu Thr Phe Thr Glu Gly Gln Lys Leu Asp Ser Ala
          20          25          30
Asp Ala Asn Phe Ser Val Trp Ile Lys Arg Cys Gln Glu Ala Gln
          35          40          45
Asn Gly Ser Glu Ser Glu Val Trp Thr His Gln Ser Lys Ile Lys
          50          55          60
Tyr Asp Trp Tyr Gln Thr Glu Ser Gln Val Val Ile Thr Leu Met
          65          70          75
Ile Lys Asn Val Gln Lys Asn Asp Val Asn Val Glu Phe Ser Glu
          80          85          90
Lys Glu Leu Ser Ala Leu Val Lys Leu Pro Ser Gly Glu Asp Tyr
          95          100          105
Asn Leu Lys Leu Glu Leu Leu His Pro Ile Ile Pro Glu Gln Ser
          110          115          120
Thr Phe Lys Val Leu Ser Thr Lys Ile Glu Ile Lys Leu Lys Lys
          125          130          135
Pro Glu Ala Val Arg Trp Glu Lys Leu Glu Gly Gln Gly Asp Val
          140          145          150
Pro Thr Pro Lys Gln Phe Val Ala Asp Val Lys Asn Leu Tyr Pro
          155          160          165
Ser Ser Ser Pro Tyr Thr Arg Asn Trp Asp Lys Leu Val Gly Glu
          170          175          180
Ile Lys Glu Glu Glu Lys Asn Glu Lys Leu Glu Gly Asp Ala Ala
          185          190          195
Leu Asn Arg Leu Phe Gln Gln Ile Tyr Ser Asp Gly Ser Asp Glu
          200          205          210
Val Lys Arg Ala Met Asn Lys Ser Phe Met Glu Ser Gly Gly Thr
          215          220          225
Val Leu Ser Thr Asn Trp Ser Asp Val Gly Lys Arg Lys Val Glu
          230          235          240
Ile Asn Pro Pro Asp Asp Met Glu Trp Lys Lys Tyr
          245          250

```

<210> 43

<211> 228

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 3149729CD1

<400> 43

```

Met Thr Met Gly Asp Lys Lys Ser Pro Thr Arg Pro Lys Arg Gln
 1          5          10          15
Ala Lys Pro Ala Ala Asp Glu Gly Phe Trp Asp Cys Ser Val Cys
          20          25          30
Thr Phe Arg Asn Ser Ala Glu Ala Phe Lys Cys Ser Ile Cys Asp
          35          40          45
Val Arg Lys Gly Thr Ser Thr Arg Lys Pro Arg Ile Asn Ser Gln
          50          55          60

```

WO 99/57144

PCT/US99/09935

```

Leu Val Ala Gln Gln Val Ala Gln Gln Tyr Ala Thr Pro Pro Pro
      65      70      75
Pro Lys Lys Glu Lys Lys Glu Lys Val Glu Lys Gln Asp Lys Glu
      80      85      90
Lys Pro Glu Lys Asp Lys Glu Ile Ser Pro Ser Val Thr Lys Lys
      95     100     105
Asn Thr Asn Lys Lys Thr Lys Pro Lys Ser Asp Ile Leu Lys Asp
     110     115     120
Pro Pro Ser Glu Ala Asn Ser Ile Gln Ser Ala Asn Ala Thr Thr
     125     130     135
Lys Thr Ser Glu Thr Asn His Thr Ser Arg Pro Arg Leu Lys Asn
     140     145     150
Val Asp Arg Ser Thr Ala Gln Gln Leu Ala Val Thr Val Gly Asn
     155     160     165
Val Thr Val Ile Ile Thr Asp Phe Lys Glu Lys Thr Arg Ser Ser
     170     175     180
Ser Thr Ser Ser Ser Thr Val Thr Ser Ser Ala Gly Ser Glu Gln
     185     190     195
Gln Asn Gln Ser Ser Ser Gly Ser Glu Ser Thr Asp Lys Gly Ser
     200     205     210
Ser Arg Ser Ser Thr Pro Lys Gly Asp Met Ser Ala Val Asn Asp
     215     220     225
Glu Ser Phe

```

<210> 44
 <211> 117
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 3705895CD1

```

<400> 44
Met Ala Ala Ala Ala Ala Ala Gly Ser Gly Thr Pro Arg Glu Glu
  1      5      10      15
Glu Gly Pro Ala Gly Glu Ala Ala Ala Ser Gln Pro Gln Ala Pro
  20      25      30
Thr Ser Val Pro Gly Ala Arg Leu Ser Arg Leu Pro Leu Ala Arg
  35      40      45
Val Lys Ala Leu Val Lys Ala Asp Pro Asp Val Thr Leu Ala Gly
  50      55      60
Gln Glu Ala Ile Phe Ile Leu Ala Arg Ala Ala Glu Leu Phe Val
  65      70      75
Glu Thr Ile Ala Lys Asp Ala Tyr Cys Cys Ala Gln Gln Gly Lys
  80      85      90
Arg Lys Thr Leu Gln Arg Arg Asp Leu Asp Asn Ala Ile Glu Ala
  95     100     105
Val Asp Glu Phe Ala Phe Leu Glu Gly Thr Leu Asp
     110     115

```

<210> 45
 <211> 252
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 003256CD1

<400> 45

```

Met Thr Pro Lys Leu Gly Arg Gly Val Leu Glu Gly Asp Asp Val
 1          5          10          15
Leu Phe Tyr Asp Glu Ser Pro Pro Pro Arg Pro Lys Leu Ser Ala
 20          25          30
Leu Ala Glu Ala Lys Lys Leu Ala Ala Ile Thr Lys Leu Arg Ala
 35          40          45
Lys Gly Gln Val Leu Thr Lys Thr Asn Pro Asn Ser Ile Lys Lys
 50          55          60
Lys Gln Lys Asp Pro Gln Asp Ile Leu Glu Val Lys Glu Arg Val
 65          70          75
Glu Lys Asn Thr Met Phe Ser Ser Gln Ala Glu Asp Glu Leu Glu
 80          85          90
Pro Ala Arg Lys Lys Arg Arg Glu Gln Leu Ala Tyr Leu Glu Ser
 95          100          105
Glu Glu Phe Gln Lys Ile Leu Lys Ala Lys Ser Lys His Thr Gly
110          115          120
Ile Leu Lys Glu Ala Glu Ala Glu Met Gln Glu Arg Tyr Phe Glu
125          130          135
Pro Leu Val Lys Lys Glu Gln Met Glu Glu Lys Met Arg Asn Ile
140          145          150
Arg Glu Val Lys Cys Arg Val Val Thr Cys Lys Thr Cys Ala Tyr
155          160          165
Thr His Phe Lys Leu Leu Glu Thr Cys Val Ser Glu Gln His Glu
170          175          180
Tyr His Trp His Asp Gly Val Lys Arg Phe Lys Cys Pro Cys
185          190          195
Gly Asn Arg Ser Ile Ser Leu Asp Arg Leu Pro Asn Lys His Cys
200          205          210
Ser Asn Cys Gly Leu Tyr Lys Trp Glu Arg Asp Gly Met Leu Lys
215          220          225
Glu Lys Thr Gly Pro Lys Ile Gly Gly Glu Thr Leu Leu Pro Arg
230          235          240
Gly Glu Glu His Ala Lys Phe Leu Asn Ser Leu Lys
245          250

```

<210> 46

<211> 530

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 156986CD1

<400> 46

```

Met Ala Lys Gly Glu Gly Ala Glu Ser Gly Ser Ala Ala Gly Leu
 1          5          10          15
Leu Pro Thr Ser Ile Leu Gln Ser Thr Glu Arg Pro Ala Gln Val
 20          25          30
Lys Lys Glu Pro Lys Lys Lys Lys Gln Gln Leu Ser Val Cys Asn
 35          40          45
Lys Leu Cys Tyr Ala Leu Gly Gly Ala Pro Tyr Gln Val Thr Gly
 50          55          60
Cys Ala Leu Gly Phe Phe Leu Gln Ile Tyr Leu Leu Asp Val Ala
 65          70          75
Gln Val Gly Pro Phe Ser Ala Ser Ile Ile Leu Phe Val Gly Arg
 80          85          90
Ala Trp Asp Ala Ile Thr Asp Pro Leu Val Gly Leu Cys Ile Ser
 95          100          105
Lys Ser Pro Trp Thr Cys Leu Gly Arg Leu Met Pro Trp Ile Ile
110          115          120

```

Phe Ser Thr Pro	Leu Ala Val Ile Ala Tyr	Phe Leu Ile Trp Phe
125	130	135
Val Pro Asp Phe	Pro His Gly Gln Thr Tyr	Trp Tyr Leu Leu Phe
140	145	150
Tyr Cys Leu Phe	Glu Thr Met Val Thr Cys	Phe His Val Pro Tyr
155	160	165
Ser Ala Leu Thr	Met Phe Ile Ser Thr Glu	Gln Thr Glu Arg Asp
170	175	180
Ser Ala Thr Ala	Tyr Arg Met Thr Val Glu	Val Leu Gly Thr Val
185	190	195
Leu Gly Thr Ala	Ile Gln Gly Gln Ile Val	Gly Gln Ala Asp Thr
200	205	210
Pro Cys Phe Gln	Asp Leu Asn Ser Ser Thr	Val Ala Ser Gln Ser
215	220	225
Ala Asn His Thr	His Gly Thr Thr Ser His	Arg Glu Thr Gln Lys
230	235	240
Ala Tyr Leu Leu	Ala Ala Gly Val Ile Val	Cys Ile Tyr Ile Ile
245	250	255
Cys Ala Val Ile	Leu Ile Leu Gly Val Arg	Glu Gln Arg Glu Pro
260	265	270
Tyr Glu Ala Gln	Gln Ser Glu Pro Ile Ala	Tyr Phe Arg Gly Leu
275	280	285
Arg Leu Val Met	Ser His Gly Pro Tyr Ile	Lys Leu Ile Thr Gly
290	295	300
Phe Leu Phe Thr	Ser Leu Ala Phe Met Leu	Val Glu Gly Asn Phe
305	310	315
Val Leu Phe Cys	Thr Tyr Thr Leu Gly Phe	Arg Asn Glu Phe Gln
320	325	330
Asn Leu Leu Leu	Ala Ile Met Leu Ser Ala	Thr Leu Thr Ile Pro
335	340	345
Ile Trp Gln Trp	Phe Leu Thr Arg Phe Gly	Lys Lys Thr Ala Val
350	355	360
Tyr Val Gly Ile	Ser Ser Ala Val Pro Phe	Leu Ile Leu Val Ala
365	370	375
Leu Met Glu Ser	Asn Leu Ile Ile Thr Tyr	Ala Val Ala Val Ala
380	385	390
Ala Gly Ile Ser	Val Ala Ala Ala Phe Leu	Leu Pro Trp Ser Met
395	400	405
Leu Pro Asp Val	Ile Asp Asp Phe His Leu	Lys Gln Pro His Phe
410	415	420
His Gly Thr Glu	Pro Ile Phe Phe Ser Phe	Tyr Val Phe Phe Thr
425	430	435
Lys Phe Ala Ser	Gly Val Ser Leu Gly Ile	Ser Thr Leu Ser Leu
440	445	450
Asp Phe Ala Gly	Tyr Gln Thr Arg Gly Cys	Ser Gln Pro Glu Arg
455	460	465
Val Lys Phe Thr	Leu Asn Met Leu Val Thr	Met Ala Pro Ile Val
470	475	480
Leu Ile Leu Leu	Gly Leu Leu Leu Phe Lys	Met Tyr Pro Ile Asp
485	490	495
Glu Glu Arg Arg	Arg Gln Asn Lys Lys Ala	Leu Gln Ala Leu Arg
500	505	510
		i
Asp Glu Ala Ser	Ser Ser Gly Cys Ser Glu	Thr Asp Ser Thr Glu
515	520	525
Leu Ala Ser Ile	Leu	
530		

<210> 47

<211> 355

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 319415CD1

<400> 47

```

Met Gly Cys Val Phe Gln Ser Thr Glu Asp Lys Cys Ile Phe Lys
 1          5          10          15
Ile Asp Trp Thr Leu Ser Pro Gly Glu His Ala Lys Asp Glu Tyr
          20          25          30
Val Leu Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe
          35          40          45
Gln Asn Arg Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly
          50          55          60
Ser Leu Leu Leu Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr
          65          70          75
Ile Cys Glu Ile Arg Leu Lys Gly Glu Ser Gln Val Phe Lys Lys
          80          85          90
Ala Val Val Leu His Val Leu Pro Glu Glu Pro Lys Glu Leu Met
          95          100          105
Val His Val Gly Gly Leu Ile Gln Met Gly Cys Val Phe Gln Ser
          110          115          120
Thr Glu Val Lys His Val Thr Lys Val Glu Trp Ile Phe Ser Gly
          125          130          135
Arg Arg Ala Lys Glu Glu Ile Val Phe Arg Tyr Tyr His Lys Leu
          140          145          150
Arg Met Ser Val Glu Tyr Ser Gln Ser Trp Gly His Phe Gln Asn
          155          160          165
Arg Val Asn Leu Val Gly Asp Ile Phe Arg Asn Asp Gly Ser Ile
          170          175          180
Met Leu Gln Gly Val Arg Glu Ser Asp Gly Gly Asn Tyr Thr Cys
          185          190          195
Ser Ile His Leu Gly Asn Leu Val Phe Lys Lys Thr Ile Val Leu
          200          205          210
His Val Ser Pro Glu Glu Pro Arg Thr Leu Val Thr Pro Ala Ala
          215          220          225
Leu Arg Pro Leu Val Leu Gly Gly Asn Gln Leu Val Ile Ile Val
          230          235          240
Gly Ile Val Cys Ala Thr Ile Leu Leu Leu Pro Val Leu Ile Leu
          245          250          255
Ile Val Lys Lys Thr Cys Gly Asn Lys Ser Ser Val Asn Ser Thr
          260          265          270
Val Leu Val Lys Asn Thr Lys Lys Thr Asn Pro Glu Ile Lys Glu
          275          280          285
Lys Pro Cys His Phe Glu Arg Cys Glu Gly Glu Lys His Ile Tyr
          290          295          300
Ser Pro Ile Ile Val Arg Glu Val Ile Glu Glu Glu Glu Pro Ser
          305          310          315
Glu Lys Ser Glu Ala Thr Tyr Met Thr Met His Pro Val Trp Pro
          320          325          330
Ser Leu Arg Ser Asp Arg Asn Asn Ser Leu Glu Lys Lys Ser Gly
          335          340          345
Gly Gly Met Pro Lys Thr Gln Gln Ala Phe
          350          355

```

<210> 48

<211> 136

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 635581CD1

<400> 48

```

Met Val Gly Gln Thr Glu Asp Asp Thr Ala Gln Gln Leu Val Pro
 1          5          10          15
Thr Cys Gly Met Lys Gly Val Gly Glu Arg Ile Val Glu Tyr Val
 20          25          30
Ser Asn Ile Pro Ala Leu Gln Arg Ala Thr Pro Lys Gly Leu Ala
 35          40          45
Ser Val Ser Pro Asp Leu Glu His Arg Gln Glu Trp Thr Tyr Ser
 50          55          60
Lys Ser Pro Leu Met Gly Lys Gly Thr Arg Leu Glu Ala Ser Glu
 65          70          75
Asn Lys Arg Ala Gly Trp Leu Ala Ala Ala Pro Glu Asn Leu Lys
 80          85          90
Tyr His Arg Gln Ile Ala Gln Gly Ala Lys Asp Tyr Glu Ile Leu
 95          100         105
Lys Lys Glu Thr Asn Lys Phe Ile Leu Arg Ile Tyr Thr His Trp
110          115         120
Ser Arg Arg Ser Ile Leu Arg Lys Gly Ser Lys Gly Met Gln Asn
125          130         135
Leu

```

<210> 49

<211> 230

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 921803CD1

<400> 49

```

Met Lys Leu Ile Val Gly Ile Gly Gly Met Thr Asn Gly Gly Lys
 1          5          10          15
Thr Thr Leu Thr Asn Ser Leu Leu Arg Ala Leu Pro Asn Cys Cys
 20          25          30
Val Ile His Gln Asp Asp Phe Phe Lys Pro Gln Asp Gln Ile Ala
 35          40          45
Val Gly Glu Asp Gly Phe Lys Gln Trp Asp Val Leu Glu Ser Leu
 50          55          60
Asp Met Glu Ala Met Leu Asp Thr Val Gln Ala Trp Leu Ser Ser
 65          70          75
Pro Gln Lys Phe Ala Arg Ala His Gly Val Ser Val Gln Pro Glu
 80          85          90
Ala Ser Asp Thr His Ile Leu Leu Leu Glu Gly Phe Leu Leu Tyr
 95          100         105
Ser Tyr Lys Pro Leu Val Asp Leu Tyr Ser Arg Arg Tyr Phe Leu
110          115         120
Thr Val Pro Tyr Glu Glu Cys Lys Trp Arg Arg Ser Thr Arg Asn
125          130         135
Tyr Thr Val Pro Asp Pro Pro Gly Leu Phe Asp Gly His Val Trp
140          145         150
Pro Met Tyr Gln Lys Tyr Arg Gln Glu Met Glu Ala Asn Gly Val
155          160         165
Glu Val Val Tyr Leu Asp Gly Met Lys Ser Arg Glu Glu Leu Phe
170          175         180
Arg Glu Val Leu Glu Asp Ile Gln Asn Ser Leu Leu Asn Arg Ser
185          190         195
Gln Glu Ser Ala Pro Ser Pro Ala Arg Pro Ala Arg Thr Gln Gly
200          205         210

```

Pro Gly Arg Gly Cys Gly His Arg Thr Ala Arg Pro Ala Ala Ser
 215 220 225
 Gln Gln Asp Ser Met
 230

<210> 50
 <211> 70
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 1250492CD1

<400> 50
 Met Thr Ile Lys Leu Arg Pro Leu Pro Phe Phe Lys Pro Lys Ser
 1 5 10 15
 Gly Asn Gln Glu Gln Gln Leu His Gly Leu Leu Ala Pro Asp Gln
 20 25 30
 Pro Gly Ser Gly Asp Ile Val Ser Leu Phe Gly Asn Cys Arg Pro
 35 40 45
 Gln Gly Val Gly Leu Ser His Phe Leu Val Leu Pro Thr Phe Pro
 50 55 60
 Ile Arg Ala Ser Ser Arg Gly Gln Val Cys
 65 70

<210> 51
 <211> 169
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 1427838CD1

<400> 51
 Met Leu Ala Phe Ser Glu Met Pro Lys Pro Pro Asp Tyr Ser Glu
 1 5 10 15
 Leu Ser Asp Ser Leu Thr Leu Ala Val Gly Thr Gly Arg Phe Ser
 20 25 30
 Gly Pro Leu His Arg Ala Trp Arg Met Met Asn Phe Arg Gln Arg
 35 40 45
 Met Gly Trp Ile Gly Val Gly Leu Tyr Leu Leu Ala Ser Ala Ala
 50 55 60
 Ala Phe Tyr Tyr Val Phe Glu Ile Ser Glu Thr Tyr Asn Arg Leu
 65 70 75
 Ala Leu Glu His Ile Gln Gln His Pro Glu Glu Pro Leu Glu Gly
 80 85 90
 Thr Thr Trp Thr His Ser Leu Lys Ala Gln Leu Leu Ser Leu Pro
 95 100 105
 Phe Trp Val Trp Thr Val Ile Phe Leu Val Pro Tyr Leu Gln Met
 110 115 120
 Phe Leu Phe Leu Tyr Ser Cys Thr Arg Ala Asp Pro Lys Thr Val
 125 130 135
 Gly Tyr Cys Ile Ile Pro Ile Cys Leu Ala Val Ile Cys Asn Arg
 140 145 150
 His Gln Ala Phe Val Lys Ala Ser Asn Gln Ile Ser Arg Leu Gln
 155 160 165
 Leu Ile Asp Thr

<210> 52
 <211> 359
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 1448258CD1

<400> 52
 Met Gly Pro Thr Lys Phe Thr Gln Thr Asn Ile Gly Ile Ile Glu
 1 5 10 15
 Asn Lys Leu Leu Glu Ala Pro Asp Val Leu Cys Leu Arg Leu Ser
 20 25 30
 Thr Glu Gln Cys Gln Ala His Glu Glu Lys Gly Ile Glu Glu Leu
 35 40 45
 Ser Asp Pro Ser Gly Pro Lys Ser Tyr Ser Ile Thr Glu Lys His
 50 55 60
 Tyr Ala Gln Glu Asp Pro Arg Met Leu Phe Val Ala Ala Val Asp
 65 70 75
 His Ser Ser Ser Gly Asp Met Ser Leu Leu Pro Ser Ser Asp Pro
 80 85 90
 Lys Phe Gln Gly Leu Gly Val Val Glu Ser Ala Val Thr Ala Asn
 95 100 105
 Asn Thr Glu Glu Ser Leu Phe Arg Ile Cys Ser Pro Leu Ser Gly
 110 115 120
 Ala Asn Glu Tyr Ile Ala Ser Thr Asp Thr Leu Lys Thr Glu Glu
 125 130 135
 Val Leu Leu Phe Thr Asp Gln Thr Asp Asp Leu Ala Lys Glu Glu
 140 145 150
 Pro Thr Ser Leu Phe Gln Arg Asp Ser Glu Thr Lys Gly Glu Ser
 155 160 165
 Gly Leu Val Leu Glu Gly Asp Lys Glu Ile His Gln Ile Phe Glu
 170 175 180
 Asp Leu Asp Lys Lys Leu Ala Leu Ala Ser Arg Phe Tyr Ile Pro
 185 190 195
 Glu Gly Cys Ile Gln Arg Trp Ala Ala Glu Met Val Val Ala Leu
 200 205 210
 Asp Ala Leu His Arg Glu Gly Ile Val Cys Arg Asp Leu Asn Pro
 215 220 225
 Asn Asn Ile Leu Leu Asn Asp Arg Gly His Ile Gln Leu Thr Tyr
 230 235 240
 Phe Ser Arg Trp Ser Glu Val Glu Asp Ser Cys Asp Ser Asp Ala
 245 250 255
 Ile Glu Arg Met Tyr Cys Ala Pro Glu Val Gly Ala Ile Thr Glu
 260 265 270
 Glu Thr Glu Ala Cys Asp Trp Trp Ser Leu Gly Ala Val Leu Phe
 275 280 285
 Glu Leu Leu Thr Gly Lys Thr Leu Val Glu Cys His Pro Ala Gly
 290 295 300
 Ile Asn Thr His Thr Thr Leu Asn Met Pro Glu Cys Val Ser Glu
 305 310 315
 Glu Ala Arg Ser Leu Ile Gln Gln Leu Leu Gln Phe Asn Pro Leu
 320 325 330
 Glu Arg Leu Gly Ala Gly Val Ala Gly Val Glu Asp Ile Lys Ser
 335 340 345
 His Pro Phe Phe Thr Pro Val Asp Trp Ala Glu Leu Met Arg
 350 355

<210> 53
 <211> 545

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1645941CD1

<400> 53

```

Met Ser Arg Lys Gln Asn Gln Lys Asp Ser Ser Gly Phe Ile Phe
 1          5          10          15
Asp Leu Gln Ser Asn Thr Val Leu Ala Gln Gly Gly Ala Phe Glu
 20          25          30
Asn Met Lys Glu Lys Ile Asn Ala Val Arg Ala Ile Val Pro Asn
 35          40          45
Lys Ser Asn Asn Glu Ile Ile Leu Val Leu Gln His Phe Asp Asn
 50          55          60
Cys Val Asp Lys Thr Val Gln Ala Phe Met Glu Gly Ser Ala Ser
 65          70          75
Glu Val Leu Lys Glu Trp Thr Val Thr Gly Lys Lys Lys Asn Lys
 80          85          90
Lys Lys Lys Asn Lys Pro Lys Pro Ala Ala Glu Pro Ser Asn Gly
 95          100          105
Ile Pro Asp Ser Ser Lys Ser Val Ser Ile Gln Glu Glu Gln Ser
 110          115          120
Ala Pro Ser Ser Glu Lys Gly Gly Met Asn Gly Tyr His Val Asn
 125          130          135
Gly Ala Ile Asn Asp Thr Glu Ser Val Asp Ser Leu Ser Glu Gly
 140          145          150
Leu Glu Thr Leu Ser Ile Asp Ala Arg Glu Leu Glu Asp Pro Glu
 155          160          165
Ser Ala Met Leu Asp Thr Leu Asp Arg Thr Gly Ser Met Leu Gln
 170          175          180
Asn Gly Val Ser Asp Phe Glu Thr Lys Ser Leu Thr Met His Ser
 185          190          195
Ile His Asn Ser Gln Gln Pro Arg Asn Ala Lys Ser Leu Ser
 200          205          210
Arg Pro Thr Thr Glu Thr Gln Phe Ser Asn Met Gly Met Glu Asp
 215          220          225
Val Pro Leu Ala Thr Ser Lys Lys Leu Ser Ser Asn Ile Glu Lys
 230          235          240
Ser Val Lys Asp Leu Gln Arg Cys Thr Val Ser Leu Ala Arg Tyr
 245          250          255
Arg Val Val Val Lys Glu Glu Met Asp Ala Ser Ile Lys Lys Met
 260          265          270
Lys Gln Ala Phe Ala Glu Leu Glu Ser Cys Leu Met Asp Arg Glu
 275          280          285
Val Ala Leu Leu Ala Glu Met Asp Lys Val Lys Ala Glu Ala Met
 290          295          300
Glu Ile Leu Leu Ser Arg Gln Lys Lys Ala Glu Leu Leu Lys Lys
 305          310          315
Met Thr His Val Ala Val Gln Met Ser Glu Gln Gln Leu Val Glu
 320          325          330
Leu Arg Ala Asp Ile Lys His Phe Val Ser Glu Arg Lys Tyr Asp
 335          340          345
Glu Asp Leu Gly Arg Val Ala Arg Phe Thr Cys Asp Val Glu Thr
 350          355          360
Leu Lys Lys Ser Ile Asp Ser Phe Gly Gln Val Ser His Pro Lys
 365          370          375
Asn Ser Tyr Ser Thr Arg Ser Arg Cys Ser Ser Val Thr Ser Val
 380          385          390
Ser Leu Ser Ser Pro Ser Asp Ala Ser Ala Ala Ser Ser Ser Thr
 395          400          405
Cys Ala Ser Pro Ser Leu Thr Ser Ala Asn Lys Lys Asn Phe
 410          415          420

```

```

Ala Pro Gly Glu Thr Pro Ala Ala Ile Ala Asn Ser Ser Gly Gln
      425                      430          435
Pro Tyr Gln Pro Leu Arg Glu Val Leu Pro Gly Asn Arg Arg Gly
      440                      445          450
Gly Gln Gly Tyr Arg Pro Gln Gly Gln Lys Ser Asn Asp Pro Met
      455                      460          465
Asn Gln Gly Arg His Asp Ser Met Gly Arg Tyr Arg Asn Ser Ser
      470                      475          480
Trp Tyr Ser Ser Gly Ser Arg Tyr Gln Ser Ala Pro Ser Gln Ala
      485                      490          495
Pro Gly Asn Thr Ile Glu Arg Gly Gln Thr His Ser Ala Gly Thr
      500                      505          510
Asn Gly Thr Gly Val Ser Met Glu Pro Ser Pro Pro Thr Pro Ser
      515                      520          525
Phe Lys Lys Gly Leu Pro Gln Arg Lys Pro Arg Thr Ser Gln Thr
      530                      535          540
Glu Ala Val Asn Ser
      545

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<210> 54
<211> 99
<212> PRT
<213> Homo sapiens

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```

<220>
<221> misc_feature
<223> Incyte clone 1646005CD1

```

```

<400> 54
Met Asn Trp Val Ala Val Leu Cys Pro Leu Gly Ile Val Trp Met
  1          5          10          15
Val Gly Asp Gln Pro Pro Gln Val Leu Ser Gln Ala Ser Ser Leu
      20          25          30
Ala Val Tyr Leu Arg Ala Ala Pro Tyr Pro Asp Val Thr Ala Lys
      35          40          45
Lys Leu Arg His Asp Thr Asn Cys Gly Phe Pro Arg Gln Gln Arg
      50          55          60
Met Ala Arg Gly His Glu Gly Arg Ala Pro Leu Leu Asp Arg Pro
      65          70          75
Thr Leu Lys Ser Arg Tyr Leu Arg Ala Asn His Lys Ile Asn Thr
      80          85          90
Phe Glu Glu Ile Thr Ala Met Pro Ser
      95

```

```

<210> 55
<211> 565
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte clone 1686561CD1

```

```

<400> 55
Met Asn Arg Ser Ile Pro Val Glu Val Asp Glu Ser Glu Pro Tyr
  1          5          10          15
Pro Ser Gln Leu Leu Lys Pro Ile Pro Glu Tyr Ser Pro Glu Glu
      20          25          30
Glu Ser Glu Pro Pro Ala Pro Asn Ile Arg Asn Met Ala Pro Asn
      35          40          45
Ser Leu Ser Ala Pro Thr Met Leu His Asn Ser Ser Gly Asp Phe
      50          55          60

```

Ser	Gln	Ala	His	Ser	Thr	Leu	Lys	Leu	Ala	Asn	His	Gln	Arg	Pro
				65					70					75
Val	Ser	Arg	Gln	Val	Thr	Cys	Leu	Arg	Thr	Gln	Val	Leu	Glu	Asp
				80					85					90
Ser	Glu	Asp	Ser	Phe	Cys	Arg	Arg	His	Pro	Gly	Leu	Gly	Lys	Ala
				95					100					105
Phe	Pro	Ser	Gly	Cys	Ser	Ala	Val	Ser	Glu	Pro	Ala	Ser	Glu	Ser
				110					115					120
Val	Val	Gly	Ala	Leu	Pro	Ala	Glu	His	Gln	Phe	Ser	Phe	Met	Glu
				125					130					135
Lys	Arg	Asn	Gln	Trp	Leu	Val	Ser	Gln	Leu	Ser	Ala	Ala	Ser	Pro
				140					145					150
Asp	Thr	Gly	His	Asp	Ser	Asp	Lys	Ser	Asp	Gln	Ser	Leu	Pro	Asn
				155					160					165
Ala	Ser	Ala	Asp	Ser	Leu	Gly	Gly	Ser	Gln	Glu	Met	Val	Gln	Arg
				170					175					180
Pro	Gln	Pro	His	Arg	Asn	Arg	Ala	Gly	Leu	Asp	Leu	Pro	Thr	Ile
				185					190					195
Asp	Thr	Gly	Tyr	Asp	Ser	Gln	Pro	Gln	Asp	Val	Leu	Gly	Ile	Arg
				200					205					210
Gln	Leu	Glu	Arg	Pro	Leu	Pro	Leu	Thr	Ser	Val	Cys	Tyr	Pro	Gln
				215					220					225
Asp	Leu	Pro	Arg	Pro	Leu	Arg	Ser	Arg	Glu	Phe	Pro	Gln	Phe	Glu
				230					235					240
Pro	Gln	Arg	Tyr	Pro	Ala	Cys	Ala	Gln	Met	Leu	Pro	Pro	Asn	Leu
				245					250					255
Ser	Pro	His	Ala	Pro	Trp	Asn	Tyr	His	Tyr	His	Cys	Pro	Gly	Ser
				260					265					270
Pro	Asp	His	Gln	Val	Pro	Tyr	Gly	His	Asp	Tyr	Pro	Arg	Ala	Ala
				275					280					285
Tyr	Gln	Gln	Val	Ile	Gln	Pro	Ala	Leu	Pro	Gly	Gln	Pro	Leu	Pro
				290					295					300
Gly	Ala	Ser	Val	Arg	Gly	Leu	His	Pro	Val	Gln	Lys	Val	Ile	Leu
				305					310					315
Asn	Tyr	Pro	Ser	Pro	Trp	Asp	Gln	Glu	Glu	Arg	Pro	Ala	Gln	Arg
				320					325					330
Asp	Cys	Ser	Phe	Pro	Gly	Leu	Pro	Arg	His	Gln	Asp	Gln	Pro	His
				335					340					345
His	Gln	Pro	Pro	Asn	Arg	Ala	Gly	Ala	Pro	Gly	Glu	Ser	Leu	Glu
				350					355					360
Cys	Pro	Ala	Glu	Leu	Arg	Pro	Gln	Val	Pro	Gln	Pro	Pro	Ser	Pro
				365					370					375
Ala	Ala	Val	Pro	Arg	Pro	Pro	Ser	Asn	Pro	Pro	Ala	Arg	Gly	Thr
				380					385					390
Leu	Lys	Thr	Ser	Asn	Leu	Pro	Glu	Glu	Leu	Arg	Lys	Val	Phe	Ile
				395					400					405
Thr	Tyr	Ser	Met	Asp	Thr	Ala	Met	Glu	Val	Val	Lys	Phe	Val	Asn
				410					415					420
Phe	Leu	Leu	Val	Asn	Gly	Phe	Gln	Thr	Ala	Ile	Asp	Ile	Phe	Glu
				425					430					435
Asp	Arg	Ile	Arg	Gly	Ile	Asp	Ile	Ile	Lys	Trp	Met	Glu	Arg	Tyr
				440					445					450
Leu	Arg	Asp	Lys	Thr	Val	Met	Ile	Ile	Val	Ala	Ile	Ser	Pro	Lys
				455					460					465
Tyr	Lys	Gln	Asp	Val	Glu	Gly	Ala	Glu	Ser	Gln	Leu	Asp	Glu	Asp
				470					475					480
Glu	His	Gly	Leu	His	Thr	Lys	Tyr	Ile	His	Arg	Met	Met	Gln	Ile
				485					490					495
Glu	Phe	Ile	Lys	Gln	Gly	Ser	Met	Asn	Phe	Arg	Phe	Ile	Pro	Val
				500					505					510
Leu	Phe	Pro	Asn	Ala	Lys	Lys	Glu	His	Val	Pro	Thr	Trp	Leu	Gln
				515					520					525
Asn	Thr	His	Val	Tyr	Ser	Trp	Pro	Lys	Asn	Lys	Lys	Asn	Ile	Leu
				530					535					540

Leu Arg Leu Leu Arg Glu Glu Glu Tyr Val Ala Pro Pro Arg Gly
 545 550 555
 Pro Leu Pro Thr Leu Gln Val Val Pro Leu
 560 565

<210> 56
 <211> 197
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 1821233CD1

<400> 56
 Met Thr Pro Thr Ser Ser Phe Val Ser Pro Pro Pro Pro Thr Ala
 1 5 10 15
 Ser Pro His Ser Asn Arg Thr Thr Pro Pro Glu Ala Ala Gln Asn
 20 25 30
 Gly Gln Ser Pro Met Ala Ala Leu Ile Leu Val Ala Asp Asn Ala
 35 40 45
 Gly Gly Ser His Ala Ser Lys Asp Ala Asn Gln Val His Ser Thr
 50 55 60
 Thr Arg Arg Asn Ser Asn Ser Pro Pro Ser Pro Ser Ser Met Asn
 65 70 75
 Gln Arg Arg Leu Gly Pro Arg Glu Val Gly Gly Gln Gly Ala Gly
 80 85 90
 Asn Thr Gly Gly Leu Glu Pro Val His Pro Ala Ser Leu Pro Asp
 95 100 105
 Ser Ser Leu Ala Thr Ser Ala Pro Leu Cys Cys Thr Leu Cys His
 110 115 120
 Glu Arg Leu Glu Asp Thr His Phe Val Gln Cys Pro Ser Val Pro
 125 130 135
 Ser His Lys Phe Cys Phe Pro Cys Ser Arg Gln Ser Ile Lys Gln
 140 145 150
 Gln Gly Ala Ser Gly Glu Val Tyr Cys Pro Ser Gly Glu Lys Cys
 155 160 165
 Pro Leu Val Gly Ser Asn Val Pro Trp Ala Phe Met Gln Gly Glu
 170 175 180
 Ile Ala Thr Ile Leu Ala Gly Asp Val Lys Val Lys Lys Glu Arg
 185 190 195
 Asp Ser

<210> 57
 <211> 321
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 1877278CD1

<400> 57
 Met Lys Glu Asp Cys Leu Pro Ser Ser His Val Pro Ile Ser Asp
 1 5 10 15
 Ser Lys Ser Ile Gln Lys Ser Glu Leu Leu Gly Leu Leu Lys Thr
 20 25 30
 Tyr Asn Cys Tyr His Glu Gly Lys Ser Phe Gln Leu Arg His Arg
 35 40 45

Glu Glu Glu Gly Thr Leu Ile Ile Glu Gly Leu Leu Asn Ile Ala
 50 55 60
 Trp Gly Leu Arg Arg Pro Ile Arg Leu Gln Met Gln Asp Asp Arg
 65 70 75
 Glu Gln Val His Leu Pro Ser Thr Ser Trp Met Pro Arg Arg Pro
 80 85 90
 Ser Cys Pro Leu Lys Glu Pro Ser Pro Gln Asn Gly Asn Ile Thr
 95 100 105
 Ala Gln Gly Pro Ser Ile Gln Pro Val His Lys Ala Glu Ser Ser
 110 115 120
 Thr Asp Ser Ser Gly Pro Leu Glu Glu Ala Glu Glu Ala Pro Gln
 125 130 135
 Leu Met Arg Thr Lys Ser Asp Ala Ser Cys Met Ser Gln Arg Arg
 140 145 150
 Pro Lys Cys Arg Ala Pro Gly Glu Ala Gln Arg Ile Arg Arg His
 155 160 165
 Arg Phe Ser Ile Asn Gly His Phe Tyr Asn His Lys Thr Ser Val
 170 175 180
 Phe Thr Pro Ala Tyr Gly Ser Val Thr Asn Val Arg Val Asn Ser
 185 190 195
 Thr Met Thr Thr Leu Gln Val Leu Thr Leu Leu Asn Lys Phe
 200 205 210
 Arg Val Glu Asp Gly Pro Ser Glu Phe Ala Leu Tyr Ile Val His
 215 220 225
 Glu Ser Gly Glu Arg Thr Lys Leu Lys Asp Cys Glu Tyr Pro Leu
 230 235 240
 Ile Ser Arg Ile Leu His Gly Pro Cys Glu Lys Ile Ala Arg Ile
 245 250 255
 Phe Leu Met Glu Ala Asp Leu Gly Val Glu Val Pro His Glu Val
 260 265 270
 Ala Gln Tyr Ile Lys Phe Glu Met Pro Val Leu Asp Ser Phe Val
 275 280 285
 Glu Lys Leu Lys Glu Glu Glu Glu Arg Glu Ile Ile Lys Leu Thr
 290 295 300
 Met Lys Phe Gln Ala Leu Arg Leu Thr Met Leu Gln Arg Leu Glu
 305 310 315
 Gln Leu Val Glu Ala Lys
 320

<210> 58

<211> 356

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1880692CD1

<400> 58

Met Glu Trp Leu Lys Ser Thr Asp Tyr Gly Lys Tyr Glu Gly Leu
 1 5 10 15
 Thr Lys Asn Tyr Met Asp Tyr Leu Ser Arg Leu Tyr Glu Arg Glu
 20 25 30
 Ile Lys Asp Phe Phe Glu Val Ala Lys Ile Lys Met Thr Gly Thr
 35 40 45
 Thr Lys Glu Ser Lys Lys Phe Gly Leu His Gly Ser Ser Gly Lys
 50 55 60
 Leu Thr Gly Ser Thr Ser Ser Leu Asn Lys Leu Ser Val Gln Ser
 65 70 75
 Ser Gly Asn Arg Arg Ser Gln Ser Ser Ser Leu Leu Asp Met Gly
 80 85 90
 Asn Met Ser Ala Ser Asp Leu Asp Val Ala Asp Arg Thr Lys Phe
 95 100 105

```

Asp Lys Ile Phe Glu Gln Val Leu Ser Glu Leu Glu Pro Leu Cys
110 115 120
Leu Ala Glu Gln Asp Phe Ile Ser Lys Phe Phe Lys Leu Gln Gln
125 130 135
His Gln Ser Met Pro Gly Thr Met Ala Glu Ala Glu Asp Leu Asp
140 145 150
Gly Gly Thr Leu Ser Arg Gln His Asn Cys Gly Thr Pro Leu Pro
155 160 165
Val Ser Ser Glu Lys Asp Met Ile Arg Gln Met Met Ile Lys Ile
170 175 180
Phe Arg Cys Ile Glu Pro Glu Leu Asn Asn Leu Ile Ala Leu Gly
185 190 195
Asp Lys Ile Asp Ser Phe Asn Ser Leu Tyr Met Leu Val Lys Met
200 205 210
Ser His His Val Trp Thr Ala Gln Asn Val Asp Pro Ala Ser Phe
215 220 225
Leu Ser Thr Thr Leu Gly Asn Val Leu Val Thr Val Lys Arg Asn
230 235 240
Phe Asp Lys Cys Ile Ser Asn Gln Ile Arg Gln Met Glu Glu Val
245 250 255
Lys Ile Ser Lys Lys Ser Lys Val Gly Ile Leu Pro Phe Val Ala
260 265 270
Glu Phe Glu Glu Phe Ala Gly Leu Ala Glu Ser Ile Phe Lys Asn
275 280 285
Ala Glu Arg Arg Gly Asp Leu Asp Lys Ala Tyr Thr Lys Leu Ile
290 295 300
Arg Gly Val Phe Val Asn Val Glu Lys Val Ala Asn Glu Ser Gln
305 310 315
Lys Thr Pro Arg Asp Val Val Met Met Glu Asn Phe His His Ile
320 325 330
Phe Ala Thr Leu Ser Arg Leu Lys Ile Ser Cys Leu Glu Ala Glu
335 340 345
Lys Lys Glu Ala Ala Ile Asn His Lys Phe Phe
350 355

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<210> 59

<211> 299

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2280456CD1

<400> 59

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Met Glu Glu Leu Leu Pro Asp Gly Gln Ile Trp Ala Asn Met Asp
1 5 10 15
Pro Glu Glu Arg Met Leu Ala Ala Ala Thr Ala Phe Thr His Ile
20 25 30
Cys Ala Gly Gln Gly Glu Gly Asp Val Arg Arg Glu Ala Gln Ser
35 40 45
Ile Gln Tyr Asp Pro Tyr Ser Lys Ala Ser Val Ala Pro Gly Lys
50 55 60
Arg Pro Ala Leu Pro Val Gln Leu Gln Tyr Pro His Val Glu Ser
65 70 75
Asn Val Pro Ser Glu Thr Val Ser Glu Ala Ser Gln Arg Leu Arg
80 85 90
Lys Pro Val Met Lys Arg Lys Val Leu Arg Arg Lys Pro Asp Gly
95 100 105
Glu Val Leu Val Thr Asp Glu Ser Ile Ile Ser Glu Ser Glu Ser
110 115 120
Gly Thr Glu Asn Asp Gln Asp Leu Trp Asp Leu Arg Gln Arg Leu
125 130 135

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Met Asn Val Gln Phe Gln Glu Asp Lys Glu Ser Ser Phe Asp Val
    140          145          150
Ser Gln Lys Phe Asn Leu Pro His Glu Tyr Gln Gly Ile Ser Gln
    155          160          165
Asp Gln Leu Ile Cys Ser Leu Gln Arg Glu Gly Met Gly Ser Pro
    170          175          180
Ala Tyr Glu Gln Asp Leu Ile Val Ala Ser Arg Pro Lys Ser Phe
    185          190          195
Ile Leu Pro Lys Leu Asp Gln Leu Ser Arg Asn Arg Gly Lys Thr
    200          205          210
Asp Arg Val Ala Arg Tyr Phe Glu Tyr Lys Arg Asp Trp Asp Ser
    215          220          225
Ile Arg Leu Pro Gly Glu Asp His Arg Lys Glu Leu Arg Trp Gly
    230          235          240
Val Arg Glu Gln Met Leu Cys Arg Ala Glu Pro Gln Ser Lys Pro
    245          250          255
Gln His Ile Tyr Val Pro Asn Asn Tyr Leu Val Pro Thr Glu Lys
    260          265          270
Lys Arg Ser Ala Leu Arg Trp Gly Val Arg Cys Asp Leu Ala Asn
    275          280          285
Gly Val Ile Pro Arg Lys Leu Pro Phe Pro Leu Ser Pro Ser
    290          295

```

<210> 60

<211> 293

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2284580CD1

<400> 60

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Met Ala Thr Phe Ser Gly Pro Ala Gly Pro Ile Leu Ser Leu Asn
    1          5          10          15
Pro Gln Glu Asp Val Glu Phe Gln Lys Glu Val Ala Gln Val Arg
    20          25          30
Lys Arg Ile Thr Gln Arg Lys Lys Gln Glu Gln Leu Thr Pro Gly
    35          40          45
Val Val Tyr Val Arg His Leu Pro Asn Leu Leu Asp Glu Thr Gln
    50          55          60
Ile Phe Ser Tyr Phe Ser Gln Phe Gly Thr Val Thr Arg Phe Arg
    65          70          75
Leu Ser Arg Ser Lys Arg Thr Gly Asn Ser Lys Gly Tyr Ala Phe
    80          85          90
Val Glu Phe Glu Ser Glu Asp Val Ala Lys Ile Val Ala Glu Thr
    95          100          105
Met Asn Asn Tyr Leu Phe Gly Glu Arg Leu Leu Glu Cys His Phe
    110          115          120
Met Pro Pro Glu Lys Val His Lys Glu Leu Phe Lys Asp Trp Asn
    125          130          135
Ile Pro Phe Lys Gln Pro Ser Tyr Pro Ser Val Lys Arg Tyr Asn
    140          145          150
Arg Asn Arg Thr Leu Thr Gln Lys Leu Arg Met Glu Glu Arg Phe
    155          160          165
Lys Lys Lys Glu Arg Leu Leu Arg Lys Lys Leu Ala Lys Lys Gly
    170          175          180
Ile Asp Tyr Asp Phe Pro Ser Leu Ile Leu Gln Lys Thr Glu Ser
    185          190          195
Ile Ser Lys Thr Asn Arg Gln Thr Ser Thr Lys Gly Gln Val Leu
    200          205          210

```

```

Arg Lys Lys Lys Lys Lys Val Ser Gly Thr Leu Asp Thr Pro Glu
215 220 225
Lys Thr Val Asp Ser Gln Gly Pro Thr Pro Val Cys Thr Pro Thr
230 235 240
Phe Leu Glu Arg Arg Lys Ser Gln Val Ala Glu Leu Asn Asp Asp
245 250 255
Asp Lys Asp Asp Glu Ile Val Phe Lys Gln Pro Ile Ser Cys Val
260 265 270
Lys Glu Glu Ile Gln Glu Thr Gln Thr Pro Thr His Ser Arg Lys
275 280 285
Lys Arg Arg Arg Ser Ser Asn Gln
290

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<210> 61
<211> 777
<212> PRT
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte clone 2779172CD1

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<400> 61
Met Val Leu Cys His Ser Phe Leu Tyr Arg Ile Leu Thr Val Gln
1 5 10 15
Gln His Gly Phe Phe Phe Gly His Asp Arg Arg Pro Ala Asp Gly
20 25 30
Glu Lys Gln Ala Ala Thr His Val Ser Leu Asp Gln Glu Tyr Asp
35 40 45
Ser Glu Ser Ser Gln Gln Trp Arg Glu Leu Glu Glu Gln Val Val
50 55 60
Ser Val Val Asn Lys Gly Val Ile Pro Ser Asn Phe His Pro Thr
65 70 75
Gln Tyr Cys Leu Asn Ser Tyr Ser Asp Asn Ser Arg Phe Pro Leu
80 85 90
Ala Val Val Glu Glu Pro Ile Thr Val Glu Val Ala Phe Arg Asn
95 100 105
Pro Leu Lys Val Leu Leu Leu Thr Asp Leu Ser Leu Leu Trp
110 115 120
Lys Phe His Pro Lys Asp Phe Ser Gly Lys Asp Asn Glu Glu Val
125 130 135
Lys Gln Leu Val Thr Ser Glu Pro Glu Met Ile Gly Ala Glu Val
140 145 150
Ile Ser Glu Phe Leu Ile Asn Gly Glu Glu Ser Lys Val Ala Arg
155 160 165
Leu Lys Leu Phe Pro His His Ile Gly Glu Leu His Ile Leu Gly
170 175 180
Val Val Tyr Asn Leu Gly Thr Ile Gln Gly Ser Met Thr Val Asp
185 190 195
Gly Ile Gly Ala Leu Pro Gly Cys His Thr Gly Lys Tyr Ser Leu
200 205 210
Ser Met Ser Val Arg Gly Lys Gln Asp Leu Glu Ile Gln Gly Pro
215 220 225
Arg Leu Asn Asn Thr Lys Glu Glu Lys Thr Ser Val Lys Tyr Gly
230 235 240
Pro Asp Arg Arg Leu Asp Pro Ile Ile Thr Glu Glu Met Pro Leu
245 250 255
Leu Glu Val Phe Phe Ile His Phe Pro Thr Gly Leu Leu Cys Gly
260 265 270
Glu Ile Arg Lys Ala Tyr Val Glu Phe Val Asn Val Ser Lys Cys
275 280 285

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Pro	Leu	Thr	Gly	Leu	Lys	Val	Val	Ser	Lys	Arg	Pro	Glu	Phe	Phe
				290					295					300
Thr	Phe	Gly	Gly	Asn	Thr	Ala	Val	Leu	Thr	Pro	Leu	Ser	Pro	Ser
				305					310					315
Ala	Ser	Glu	Asn	Cys	Ser	Ala	Tyr	Lys	Thr	Val	Val	Thr	Asp	Ala
				320					325					330
Thr	Ser	Val	Cys	Thr	Ala	Leu	Ile	Ser	Ser	Ala	Ser	Ser	Val	Asp
				335					340					345
Phe	Gly	Ile	Gly	Thr	Gly	Ser	Gln	Pro	Glu	Val	Ile	Pro	Val	Pro
				350					355					360
Leu	Pro	Asp	Thr	Val	Leu	Leu	Pro	Gly	Ala	Ser	Val	Gln	Leu	Pro
				365					370					375
Met	Trp	Leu	Arg	Gly	Pro	Asp	Glu	Glu	Gly	Val	His	Glu	Ile	Asn
				380					385					390
Phe	Leu	Phe	Tyr	Tyr	Glu	Ser	Val	Lys	Lys	Gln	Pro	Lys	Ile	Arg
				395					400					405
His	Arg	Ile	Leu	Arg	His	Thr	Ala	Ile	Ile	Cys	Thr	Ser	Arg	Ser
				410					415					420
Leu	Asn	Val	Arg	Ala	Thr	Val	Cys	Arg	Ser	Asn	Ser	Leu	Glu	Asn
				425					430					435
Glu	Glu	Gly	Arg	Gly	Asn	Met	Leu	Val	Val	Phe	Val	Asp	Val	Glu
				440					445					450
Asn	Thr	Asn	Thr	Ser	Glu	Ala	Gly	Val	Lys	Glu	Phe	His	Ile	Val
				455					460					465
Gln	Val	Ser	Ser	Ser	Ser	Lys	His	Trp	Lys	Leu	Gln	Lys	Ser	Val
				470					475					480
Asn	Leu	Ser	Glu	Asn	Lys	Asp	Thr	Lys	Leu	Ala	Ser	Arg	Glu	Lys
				485					490					495
Gly	Lys	Phe	Cys	Phe	Lys	Ala	Ile	Arg	Cys	Glu	Lys	Glu	Glu	Ala
				500					505					510
Ala	Thr	Gln	Ser	Ser	Glu	Lys	Tyr	Thr	Phe	Ala	Asp	Ile	Ile	Phe
				515					520					525
Gly	Asn	Glu	Gln	Ile	Ile	Ser	Ser	Ala	Ser	Pro	Cys	Ala	Asp	Phe
				530					535					540
Phe	Tyr	Arg	Ser	Leu	Ser	Ser	Glu	Leu	Lys	Lys	Pro	Gln	Ala	His
				545					550					555
Leu	Pro	Val	His	Thr	Glu	Lys	Gln	Ser	Thr	Glu	Asp	Ala	Val	Arg
				560					565					570
Leu	Ile	Gln	Lys	Cys	Ser	Glu	Val	Asp	Leu	Asn	Ile	Val	Ile	Leu
				575					580					585
Trp	Lys	Ala	Tyr	Val	Val	Glu	Asp	Ser	Lys	Gln	Leu	Ile	Leu	Glu
				590					595					600
Gly	Gln	His	His	Val	Ile	Leu	Arg	Thr	Ile	Gly	Lys	Glu	Ala	Phe
				605					610					615
Ser	Tyr	Pro	Gln	Lys	Gln	Glu	Pro	Pro	Glu	Met	Glu	Leu	Leu	Lys
				620					625					630
Phe	Phe	Arg	Pro	Glu	Asn	Ile	Thr	Val	Ser	Ser	Arg	Pro	Ser	Val
				635					640					645
Glu	Gln	Leu	Ser	Ser	Leu	Ile	Lys	Thr	Ser	Leu	His	Tyr	Pro	Glu
				650					655					660
Ser	Phe	Asn	His	Pro	Phe	His	Gln	Lys	Ser	Leu	Cys	Leu	Val	Pro
				665					670					675
Val	Thr	Leu	Leu	Leu	Ser	Asn	Cys	Ser	Lys	Ala	Asp	Val	Asp	Val
				680					685					690
Ile	Val	Asp	Leu	Arg	His	Lys	Thr	Thr	Ser	Pro	Glu	Ala	Leu	Glu
				695					700					705
Ile	His	Gly	Ser	Phe	Thr	Trp	Leu	Gly	Gln	Thr	Gln	Tyr	Lys	Leu
				710					715					720
Gln	Leu	Lys	Ser	Gln	Glu	Ile	His	Ser	Leu	Gln	Leu	Lys	Ala	Cys
				725					730					735
Phe	Val	His	Thr	Gly	Val	Tyr	Asn	Leu	Gly	Thr	Pro	Arg	Val	Phe
				740					745					750
Ala	Lys	Leu	Ser	Asp	Gln	Val	Thr	Val	Phe	Glu	Thr	Ser	Gln	Gln
				755					760					765

Asn Ser Met Pro Ala Leu Ile Ile Ile Ser Asn Val
770 775

<210> 62
<211> 97
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte clone 3279329CD1

<400> 62
Met Pro Pro Gly Thr Val Leu Arg Tyr Val Gln Cys Leu Phe Leu
1 5 10 15
Asp Leu Cys Ile Cys His Glu Ala Pro Cys Gly Leu Cys Met Lys
20 25 30
Leu Leu Leu Cys Phe Trp Val Asn Arg Cys Ala Cys Gln Leu Ala
35 40 45
Cys Val Leu Ser Lys Phe His Lys Leu Lys Val Phe Lys Gly Cys
50 55 60
Val Val Ser Glu Leu Tyr Val Ser Phe Leu Ser Leu Tyr Leu Gln
65 70 75
Arg Val Arg Asn Glu Ile Tyr Thr Ser Lys Val Ser Leu Ile Asn
80 85 90
Met Ala Phe Cys Phe Ser Met
95

<210> 63
<211> 308
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte clone 3340290CD1

<400> 63
Met Ser Val Ser Gly Leu Lys Ala Glu Leu Lys Phe Leu Ala Ser
1 5 10 15
Ile Phe Asp Lys Asn His Glu Arg Phe Arg Ile Val Ser Trp Lys
20 25 30
Leu Asp Glu Leu His Cys Gln Phe Leu Val Pro Gln Gln Gly Ser
35 40 45
Pro His Ser Leu Pro Pro Pro Leu Thr Leu His Cys Asn Ile Thr
50 55 60
Glu Ser Tyr Pro Ser Ser Ser Pro Ile Trp Phe Val Asp Ser Glu
65 70 75
Asp Pro Asn Leu Thr Ser Val Leu Glu Arg Leu Glu Asp Thr Lys
80 85 90
Asn Asn Asn Leu Asn Gly Thr Thr Glu Glu Val Thr Ser Glu Glu
95 100 105
Glu Glu Glu Glu Glu Glu Met Ala Glu Asp Ile Glu Asp Leu Asp
110 115 120
His Tyr Glu Met Lys Glu Glu Glu Pro Ile Ser Gly Lys Lys Ser
125 130 135
Glu Asp Glu Gly Ile Glu Lys Glu Asn Leu Ala Ile Leu Glu Lys
140 145 150
Ile Arg Lys Thr Gln Arg Gln Asp His Leu Asn Gly Ala Val Ser
155 160 165

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Gly Ser Val Gln Ala Ser Asp Arg Leu Met Lys Glu Leu Arg Asp
170 175 180
Ile Tyr Arg Ser Gln Ser Tyr Lys Thr Gly Ile Tyr Ser Val Glu
185 190 195
Leu Ile Asn Asp Ser Leu Tyr Asp Trp His Val Lys Leu Gln Lys
200 205 210
Val Asp Pro Asp Ser Pro Leu His Ser Asp Leu Gln Ile Leu Lys
215 220 225
Glu Lys Glu Gly Ile Glu Tyr Ile Leu Leu Asn Phe Ser Phe Lys
230 235 240
Asp Asn Phe Pro Phe Asp Pro Pro Phe Val Arg Val Val Leu Pro
245 250 255
Val Leu Ser Gly Gly Tyr Val Leu Gly Gly Gly Ala Leu Cys Met
260 265 270
Glu Leu Leu Thr Lys Gln Asn Gln Tyr Asn Leu Ala Arg Ala Gln
275 280 285
Gln Ser Tyr Asn Ser Ile Val Gln Ile His Glu Lys Asn Gly Trp
290 295 300
Tyr Thr Pro Pro Lys Glu Asp Gly
305

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<210> 64
<211> 290
<212> PRT
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte clone 3376404CD1

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<400> 64
Met Arg Arg Pro Ala Ala Val Pro Leu Leu Leu Leu Cys Phe
1 5 10 15
Gly Ser Gln Arg Ala Lys Ala Ala Thr Ala Cys Gly Arg Pro Arg
20 25 30
Met Leu Asn Arg Met Val Gly Gly Gln Asp Thr Gln Glu Gly Glu
35 40 45
Trp Pro Trp Gln Val Ser Ile Gln Arg Asn Gly Ser His Phe Cys
50 55 60
Gly Gly Ser Leu Ile Ala Glu Gln Trp Val Leu Thr Ala Ala His
65 70 75
Cys Phe Arg Asn Thr Ser Glu Thr Ser Leu Tyr Gln Val Leu Leu
80 85 90
Gly Ala Arg Gln Leu Val Gln Pro Gly Pro His Ala Met Tyr Ala
95 100 105
Arg Val Arg Gln Val Glu Ser Asn Pro Leu Tyr Gln Gly Thr Ala
110 115 120
Ser Ser Ala Asp Val Ala Leu Val Glu Leu Glu Ala Pro Val Pro
125 130 135
Phe Thr Asn Tyr Ile Leu Pro Val Cys Leu Pro Asp Pro Ser Val
140 145 150
Ile Phe Glu Thr Gly Met Asn Cys Trp Val Thr Gly Trp Gly Ser
155 160 165
Pro Ser Glu Glu Asp Leu Leu Pro Glu Pro Arg Ile Leu Gln Lys
170 175 180
Leu Ala Val Pro Ile Ile Asp Thr Pro Lys Cys Asn Leu Leu Tyr
185 190 195
Ser Lys Asp Thr Glu Phe Gly Tyr Gln Pro Lys Thr Ile Lys Asn
200 205 210
Asp Met Leu Cys Ala Gly Phe Glu Glu Gly Lys Lys Asp Ala Cys
215 220 225
Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Val Gly Gln Ser
230 235 240

```

Trp	Leu	Gln	Ala	Gly	Val	Ile	Ser	Trp	Gly	Glu	Gly	Cys	Ala	Arg
				245					250					255
Gln	Asn	Arg	Pro	Gly	Val	Tyr	Ile	Arg	Val	Thr	Ala	His	His	Asn
				260					265					270
Trp	Ile	His	Arg	Ile	Ile	Pro	Lys	Leu	Gln	Phe	Gln	Pro	Ala	Arg
				275					280					285
Leu	Gly	Gly	Gln	Lys										
				290										

<210> 65
 <211> 198
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 4173111CD1

Met	Glu	Met	Ser	Gly	Leu	Ser	Phe	Ser	Glu	Met	Glu	Gly	Cys	Arg
1				5					10					15
Asn	Leu	Leu	Gly	Leu	Leu	Asp	Asn	Asp	Glu	Ile	Met	Ala	Leu	Cys
				20					25					30
Asp	Thr	Val	Thr	Asn	Arg	Leu	Val	Gln	Pro	Gln	Asp	Arg	Gln	Asp
				35					40					45
Ala	Val	His	Ala	Ile	Leu	Ala	Tyr	Ser	Gln	Ser	Ala	Glu	Glu	Leu
				50					55					60
Leu	Arg	Arg	Arg	Lys	Val	His	Arg	Glu	Val	Ile	Phe	Lys	Tyr	Leu
				65					70					75
Ala	Thr	Gln	Gly	Ile	Val	Ile	Pro	Pro	Ala	Thr	Glu	Lys	His	Asn
				80					85					90
Leu	Ile	Gln	His	Ala	Lys	Asp	Tyr	Trp	Gln	Lys	Gln	Pro	Gln	Leu
				95					100					105
Lys	Leu	Lys	Glu	Thr	Pro	Glu	Pro	Val	Thr	Lys	Thr	Glu	Asp	Ile
				110					115					120
His	Leu	Phe	Gln	Gln	Gln	Val	Lys	Glu	Asp	Lys	Lys	Ala	Glu	Lys
				125					130					135
Val	Asp	Phe	Arg	Arg	Leu	Gly	Glu	Glu	Phe	Cys	His	Trp	Phe	Phe
				140					145					150
Gly	Leu	Leu	Asn	Ser	Gln	Asn	Pro	Phe	Leu	Gly	Pro	Pro	Gln	Asp
				155					160					165
Glu	Trp	Gly	Pro	Gln	His	Phe	Trp	His	Asp	Val	Lys	Leu	Arg	Phe
				170					175					180
Tyr	Tyr	Asn	Thr	Ser	Glu	Gln	Asn	Val	Met	Gly	Leu	Thr	Met	Glu
				185					190					195
Pro	Glu	Ser												

<210> 66
 <211> 789
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 001106CB1

<400> 66
 atatatacgt atatacccct cttgcccttg aaggccggaa gtcggtctta cagataaaaag 60
 cgaaacagga agtcccgcgc cttatggaa agtaaatggt agctcggaag ggtcaaaaga 120
 gtccgcggtt tcgcccgcgtg agtgctttt tgcggctggg gaggtctacg cttctagagc 180


```

ttgagccagc ggggcgaccc tgcagtggca ggactcggca ccgcgccctc caccgccggt 240
tgggtggcctg cgtgacagtt tcctcccgtc gacatcgaaa ggaagccgga cgtgggagg 300
cagagagctt catcgagta ggaatggcag ccccatctat gaaggaaaga caggtctgct 360
ggggggcccg ggtgagtagc tggaagtgtt tagatgagaa cttagaggat gcttctcaat 420
gcaagaagtt aagaagctct ttcgaatcaa gttgtcccca acagtggata aaatattttg 480
ataaaagaag agactactta aaattcaaaag aaaaatttga agcaggacaa tttgagcctt 540
cagaacaac tgcaaatcc taggctgttc ataaagattg aaagtattct ttctggacat 600
tgaaaaagct ccactgacta tggaaacagta atagtttgaa tcatagttaa catcaatact 660
tgttccctat atacgacact tgataattaa gatgatcaag aaccagaaga tctgtgaaga 720
aatgaaataa aatggtattt agtaagaaat ctctatttta agaaaaaag taaaacctgt 780
tataaacia

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<210> 67

<211> 1117

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<223> Incyte clone 004586CB1

<400> 67

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gccagagcgc ttcggccttc ccgacctctc cccggagccc cgggcctccc cggctgcttc 60
cctgagtcct tcctcctctc gccagagccc gagcgcccct cggagaccct cggctttccc 120
cgtccgctct cccggaggca gcgcggggct ataggacgaa gttatacgga agcgtctcct 180
cattgatgga gatggtgctg gagatgatcg gagaattaat ctgctagtga agagtttcat 240
taaatggtgc aactctgggt cccaggaaga gggatatagc cagtaccaac gtatgctgag 300
cacgctgtct caatgtgaat tttcaatggg caaaacttta ctagtatatg atatgaatct 360
cagagaaatg gaaaattatg aaaaaattta caaggaaata gaatgtagca tagctggagc 420
acatgaaaaa attgctgagt gcaaaaagca aattcttcaa gcaaaacgaa tacgaaaaaa 480
tcgccaagaa tatgatgctt tggcaaaagt gattcagcac catccagaca ggcagtagac 540
attaaaggaa ctagaggctc tgggaaaaaga attagagcat ctttcacaca ttaaagaaag 600
tgttgaagat aagctggaat tgagacggaa acagtttcat gttcttctta gtaccatcca 660
tgaaacttcag caaacattgg aaaatgatga aaactctca gaggtagaag aagctcagga 720
agcaagcatg gaaacagatc ctaagccata gacaggctaa ttgcccacca ctcccaggaa 780
tattgaaata gctacatgac cataatgtgt ttaaagtgtg gtatgctctt gagatattta 840
aagttttggc agtaaaatac tctgttttta agtatgaatg tatttcattc atatttcctc 900
tcacaaagga aaatgacttc agtatagatt tgtttttatt aaaatgcatt ttttattctt 960
aagtggtagg aagcaacatc caaaaatgct taataaaatg cttttaagct gcaaaaaaga 1020

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annnaaanga gcantnanng ntggggggcnc cnnngtaaa ananaaaggg gnggnccccc 1080
ggnntanntg aancccatcn nccccggga ttttaatt

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<210> 68

<211> 1628

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<223> Incyte clone 052927CB1

<400> 68

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ggcggcgggc acgactgcag ctccggagggt agcggcctgg cgaggggacgg gccggctgcc 60
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<223> Incyte clone 082843CB1

<400> 69

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<211> 1864

<212> DNA
<213> Homo sapiens

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<223> Incyte clone 322349CB1

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<212> DNA
<213> Homo sapiens

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<211> 3685

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<213> Homo sapiens

<220>

<221> misc feature

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<400> 72

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<210> 74

<211> 1578

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1760185CB1

<400> 74

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tttgcttgaa aaaaaaaa 1578

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<210> 75
 <211> 1624
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <223> Incyte clone 1805061CB1

<400> 75
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<210> 76
 <211> 1675
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <223> Incyte clone 1850120CB1

<400> 76
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<210> 77

<211> 1319

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1852290CB1

<400> 77

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cttctg+ygc ccttaatgcc aacttttgt cctggaagag tcgtaccaag tacaccatta 360
caccagtga gatgaggaag tctggggggc gagaccacac aggccgaatc cgggtgcatg 420
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<210> 78

<211> 1113

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1944530CB1

<400> 78

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<210> 79

<211> 1963

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2019742CB1

<400> 79

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<210> 80
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 <212> DNA
 <213> Homo sapiens

<220>
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 <223> Incyte clone 2056042CB1

<400> 80
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 <211> 1325
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 2398682CB1

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 <211> 1579
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <223> Incyte clone 2518753CB1

<400> 82
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 <223> Incyte clone 2709055CB1

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<211> 3963

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2724537CB1

<400> 84

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<213> Homo sapiens

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<221> misc_feature

<223> Incyte clone 025818CB1

<400> 85

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<211> 2077

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<223> Incyte clone 438283CB1

<400> 86

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<211> 2358

<212> DNA
<213> Homo sapiens

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<221> misc_feature
<223> Incyte clone 619699CB1

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<211> 1978
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
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<213> Homo sapiens

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<223> Incyte clone 839651CB1

<400> 89

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<212> DNA

<213> Homo sapiens

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<400> 92

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<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2076520CB1

<400> 97

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<213> Homo sapiens

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 <213> Homo sapiens

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ctaaaaaaaa aa 2232

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<210> 101
 <211> 1620
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 2495790CB1

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<400> 101
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<210> 102
 <211> 608
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 2661254CB1

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jttgtagcat ggagggcccg gcatcgctga cccccacgcc gagggcttgc cgttttccc 480
gaggacgtgg acttttgtga gacaagaggc ggctccccag cctgggtttc catgtgacct 540
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aaaaaaaaa 608

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<210> 103
 <211> 3257
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 2674047CB1

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<400> 103
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agagaggatg ttctagagcc atggttgaaa ttgaattgtt cagggttctt ggaaatcttg 180
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ctttccaaaa tagcagc 3257

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<210> 104

<211> 1945

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<223> Incyte clone 2762174CB1

<400> 104

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cccattgtgac atatgtggcc caatatgtga agatacctta cacctggcta aataccatgg 180
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tacagacttt gaccagcacc agaaccagcc caatggaggg aaacttttcc caaggaaagga 300
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gaaaggtagg agagactttt cagccacatc tggccttctt cagcatcagg cctctctcag 420
cagcatgaag ccccacaaga gcactaagct tgtgagtggc tttctcatgg gacagaggta 480
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<210> 105

<211> 1829

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2765991CB1

<400> 105

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gtttatcaaa gcgaaatgtg tctttgactc gaagtcacag tgttgaggcg ccattgcaga 360
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gcaactccag cttgggtgac agagtgagc                                     1829

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<210> 106
 <211> 1353
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 2775157CB1

<400> 106
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 ggccgagtgcc ccagtgaccc ttccacgggg gtagctttta ctccgcactc tcagccccctg 180
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<210> 107
 <211> 1025
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte clone 2918375CB1

<400> 107
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<210> 108
<211> 3641
<212> DNA
<213> Homo sapiens

<220>
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<223> Incyte clone 3149729CB1

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<210> 109

<211> 699

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 3705895CB1

<400> 109

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<210> 110

<211> 2186

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 003256CB1

<400> 110

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<210> 111

<211> 2133

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 156986CB1

<400> 111

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 <211> 1649
 <212> DNA
 <213> Homo sapiens

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 <223> Incyte clone 319415CB1

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 <213> Homo sapiens

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 <213> Homo sapiens
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<210> 116

<211> 1010

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1427838CB1

<400> 116

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tgagtgaactc ttttaacgctt gccgtgggaa caggaagatt ttcgggacca ttgcacagag 180
catggagaat gatgaacttc cgtcagcgga tgggatggat tggagtggga ttgtatctgt 240
tagccagtgc agcagcattt tactatgttt tggaaatcag tgagacttac aacaggctgg 300
ccttggaaac cattcaacag caccctgagg agcccttga aggaacacac tggacacact 360
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gtactgtat catccctata tgcttgccag ttatttgcaa tcgccaccag gcatttgtca 540
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agaaattttt cctttgggga aaaaaatgaa tatgaacatt tccattgtgt taagtgtaaa 960
aagggtccaga catgatcata aaatttaaat ttatataaat aaaaaaaaaa 1010

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<210> 117

<211> 2059

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1448258CB1

<400> 117

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aggggtcag atgactcagt gccagttatt tcatttaaag atgctgcttt tgatgatgtc 60
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acaagagaag ctgcagcaat gggacctact aagtttacac aaactaatat agggataata 180
gaaaataaac tcttgaagc ccctgatgtt ttatgcctca ggcttagtac tgaacaatgc 240
caagcacatg aggagaaagg catagaggaa ctgagtgtac cctctgggcc caaatcctat 300
agtataacag agaaacacta tgcacaggag gatcccagga tgttatttgt agcagctgtt 360
gatcatagta gtccaggaga tatgtctttg ttaccagct cagatcctaa gtttcaagga 420
cttgagtggt ttgagtcagc agtaactgca aacaacacag aagaaagctt attccgtatt 480
tgtagtccac tctcaggtgc taatgaatat attgcaagca cagacacttt aaaaacagaa 540

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gaagtattgc tgtttacaga tcagactgat gatttggcta aagaggaacc aacttcttta 600
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atacatcaga tttttgagga ccttgataaa aaattagcac tagcctccag gttttacatc 720
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gaaacattaa aaaaaaaaaa

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<210> 118

<211> 2273

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1645941CB1

<400> 118

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gctagcgagc agaatttoga acagcaggat ttctgtatctt ttgcttccaa ctgcacactt 360
ccgttgccca ctttttaaatc agagatacct acactcaaaa ccagagacaag gcaaaaggat 420
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aggattcatc aggattcatt tttgatttgc agtccaatac cgtactggcc cagggaggag 540
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cattcatgga aggtagtgc agtgaaagtac tcaaagaatg gacagtaaca ggcaagaaaa 720
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<210> 119
 <211> 1772
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <223> Incyte clone 1646005CB1

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<400> 119
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<210> 120
 <211> 2260
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <223> Incyte clone 1686561CB1

<400> 120

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atcagaacca tacccaagtc agttgtctgaa accaatccca gaatatcccc cggaagagga 180
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<210> 121

<211> 1602

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1821233CB1

<400> 121

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<210> 122

<211> 1655

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1877278CB1

<400> 122

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<210> 123

<211> 2225

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 1880692CB1

<400> 123

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cttcc 2225

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<210> 124

<211> 1516

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2280456CB1

<400> 124

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```

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aaattcaaaa aaaaaa 1516

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<210> 125

<211> 1635

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2284580CB1

<400> 125

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<210> 126

<211> 2673

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 2779172CB1

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<210> 127

<211> 2206

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 3279329CB1

<400> 127

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gagatttata catccaaagt tagtctgata aatatggctt tttgtttctc catgtaacct 360

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<210> 128

<211> 1426

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 3340290CB1

<400> 128

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<210> 129

<211> 1703

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte clone 3376404CB1

<400> 129

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